INDOLIZINES : WITH SPECIAL REFERENCE TO THE ACTION OF ELECTROPHILIC REAGENTS

Martin Fraser

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INDOLIZINES - WITH SPECIAL REFERENCE

TO THE ACTION OF

ELECTROPHILIC REAGENTS

being a Thesis presented by

MARTIN FRASER

to the University of St. Andrews in

application for the degree of Ph.D.

CERTIFICATE

I certify that Martin Fraser has spent nine terms at research work under my direction, that he has fulfilled the conditions of Ordinance No. 16 (St. Andrews) and is qualified to submit the accompanying Thesis in application for the degree of Ph.D.

Director of Research.

October 1962.

DECLARATION

I hereby declare that the following Thesis is a record of the results of experiments carried out by me, and further that the Thesis is my own composition and has not previously been presented for a higher degree.

The research was carried out in the Department of Chemistry, United College, University of St. Andrews, under the direction of Dr. D.H. Reid.

October 1962.

UNIVERSITY CAREER

I first matriculated in the United College of St. Salvator and St. Leonard, University of St. Andrews, in October 1955, and subsequently graduated B.Sc. with Second Class Honours in Chemistry in June 1959.

I was admitted as a Research Student in the Department of Chemistry, United College, St. Andrews, in September 1959.

I was awarded a Research Studentship by the Department of Scientific and Industrial Research for the whole of my period as a Research Student.

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I am grateful to the Department of Scientific and Industrial Research for the award of a Research Studentship during the period of my research programme.

For helpful discussion I thank Mr. B. Holley, Mr. R. Boyd and Mr. R.G. Sutherland. I should also like to thank the members of the Technical Staff, in particular Mr. R.M. Zochowski for recording the infra-red spectra, and Messrs. R. Harris and A. Watson for photographic assistance.

I thank Professor John Read, F.R.S., for his permission to carry out these researches in the Chemistry Department, St. Andrews.

University of St. Andrews.
October, 1962.

EXPLANATORY NOTE

This thesis comprises three parts, A, B and C. Each Part is divided into sections prefixed by Roman numerals, and some of these sections have been further divided into sub-sections, prefixed by arabic numerals. Reference to another place in the thesis is thus made (in parenthesis) by a combination of a capital letter, a Roman numeral, and, if necessary, an arabic numeral, e.g. (AIV_2), The Concept of Aromaticity. In Part C the large sections on Ethoxymethyleneindolizinium salts CIII, monomethine dyes from Indolizines CV and Preparation of Indolizine Aldehydes CVI, have been broken down into smaller subsidiary sections, prefixed by a small letter, e.g. (CIII a_1), 3-Ethoxymethylene-2-methylindolizinium perchlorate.

Structural formulae and figures (with Arabic numerals) and tables (with Roman numerals) are numbered independently within each Part. The proton magnetic resonance spectra are denoted by small letters. Sub-division of formulae numbers with small letters (e.g. 9a and b, Part B) is used to distinguish alternative canonical structures, whereas sub-division of formulae numbers with capital letters (e.g. 22A and 22B, Part B) is used to distinguish between alternative structural isomers. Reference to the chemical literature is consecutive throughout the thesis, and each reference is indicated by a number in superscript, a key to which is given at the end of the thesis.

Part A briefly surveys the synthetic routes, properties and relationship of indolizine to other aromatic systems.

Part B is a discussion of the results achieved in the course of investigation centred on the reactions of indolizines with electrophilic reagents.

Part C is devoted to a description of experimental details, and is the compliment to Part B.

A number of visible absorption spectra are shown on Plates at the end of the thesis.

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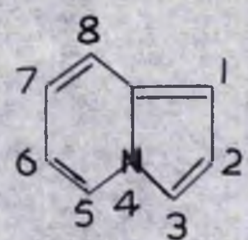
[illegible] A

AI <u>Indolizine: Introduction</u>

Indolizine was first synthesised by Scholtz[1] in 1912 who proposed at that time the presently accepted ring structure (1). A number of alternative names and systems of numbering have been suggested for the heterocycle. These include pyrindole, pyrrodine, pyrrocoline, 8 pyrrolopyridine and pyrrolo [1,2-a] pyridine. It is proposed to use the name indolizine and the numbering as shown in (1), in accordance with the recommendations of the I.U.P.A.C. Direct support for Scholtz's formulation of the structure of indolizine followed from its catalytic reduction[2] showing the presence of four double bonds, to a derivative identical with δ-coniceine (2) (octahydroindolizine), which on degradation with cyanogen bromide yielded dl coniine (2-n-propylpiperidine). Further evidence substantiating this formulation of indolizine arises from consideration of numerous syntheses described below.

(1)



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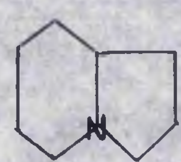


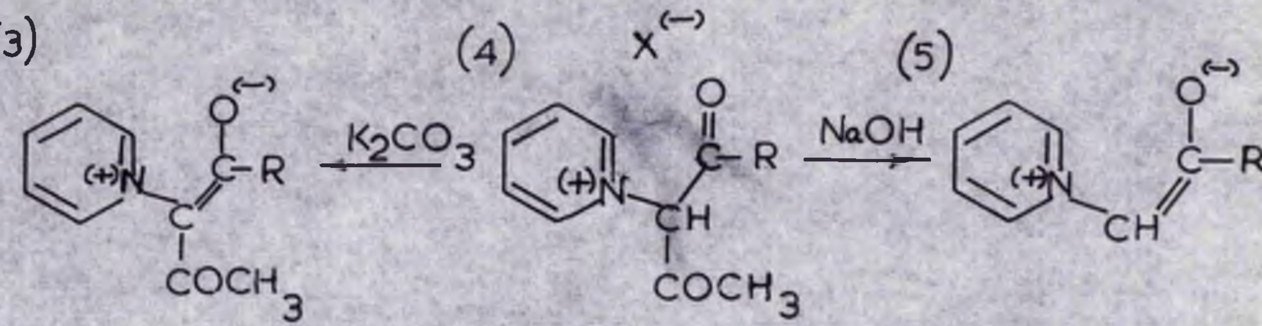
AII Indolizines: Synthetic Routes.

(a) The Tschitschibabin Synthesis.

The synthesis which has formed the basis for the formation of most of the alkyl - and aryl - derivatives of indolizine is that of Tschitschibabin,[3] in which a methyl (one) pyridine is quaternised with an α-halocarbonyl compound and the resulting quaternary salt cyclised with alkali. The synthesis is of little value for the preparation of indolizine itself, as yields of only 1% are obtained by alkali treatment of the quaternary salt which is formed between 2-picoline and bromoacetaldehyde, but yields of 2-alkyl and more so 2-arylindolizines are very much better.

Optimum yields are obtained using (a) bromo rather than chloroketones,[4] in which case the use of solvent as a moderator[5] to the more exothermic reactions is desirable; (b) sodium carbonate rather than sodium or potassium hydroxide for cyclisation of the quaternary pyridinium salt. The theoretical reason for the latter modification and an explanation for the failure to extend the reaction to include the use of α-chloroacetylacetone, α-bromobenzoylacetone, ethyl-α-chloroacetoacetate or ethyl-α-bromobenzoylacetate,[6] depends on the enol-betaine[7,8,9], e.g. (3) or (4), which results from the treatment of quaternary salt (5) with base. The nature of the enol betaine depends on the nature of the quaternary salt and the strength of the base; stronger base causes acyl or carbalkoxy cleavage.

(3) (4) (5)

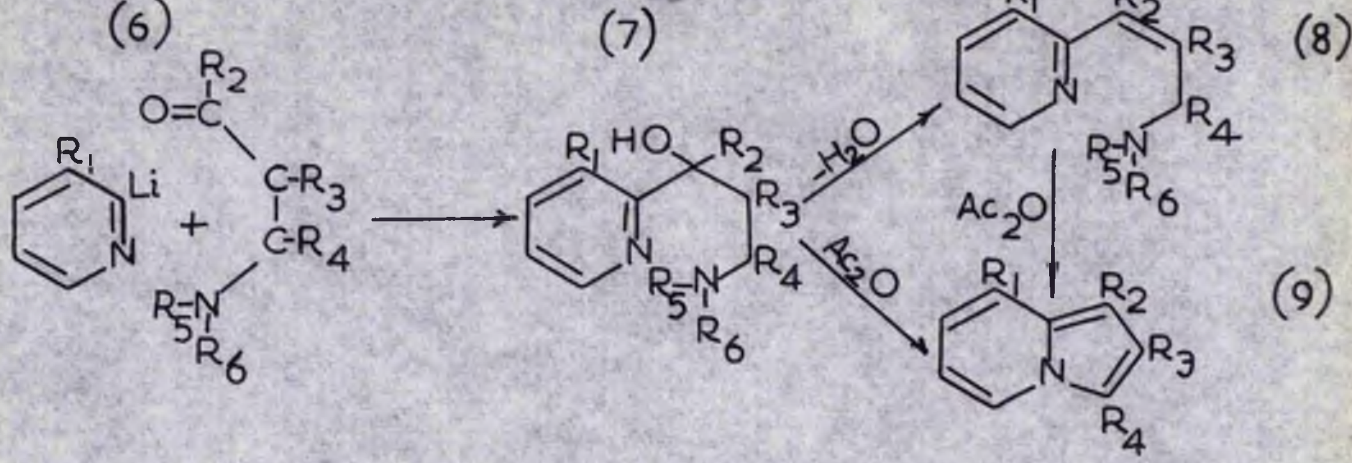


Exceptionally ethyl bromopyruvate[10] condensed with 2-picoline to give in moderate yield indolizine-2-carboxylic acid, and ω-chloro*iso*nitrosoacetophenone with 2-picoline gave 3-nitroso-2-phenylindolizine.[11]

The yield of the indolizine was also adversely affected when haloketones in which either the halogen[12] or the carbonyl[13] groups are hindered, or when 6-substituted 2-picolines are employed.[3,5,14.] Unaccountably, substitution of quinaldine for 2-picoline in the reaction with chloroacetone or ω-bromoacetophenone merely produced quinaldine hydrohalides.[6]

(b) Borrett's Synthesis.

Although 1-substituted indolizines may be prepared by the Tschitschibabin synthesis e.g. 2-methyl-1-phenyl (CI) or 1,2-dimethylindolizine (CI). A more general synthesis of 1-substituted indolizines, and the second most extensively used synthetic route is that of Borrett.[15,16,17,18.] The method is best described by reference to the following reaction scheme.



Ketones of type (6) react with derivatives of pyridyl lithium to give carbinols of type (7). Dehydration of (7) with sulphuric acid yields alkenes (8). Refluxing either (7) or (8) for several hours with acetic anhydride produced (9) in 35-60% yields. When R_4 in (8) or (9) is hydrogen, acetylation of the reactive 3- position of the indolizine occurs during cyclisation. The reactions are cleaner and slower and the yields of (9) higher when R_2 is alkyl instead of aryl. Investigation[18] of the reaction and its side products has shown that cyclisation of (7) does not proceed via the alkene structures (8), but involves an acetoxy compound.

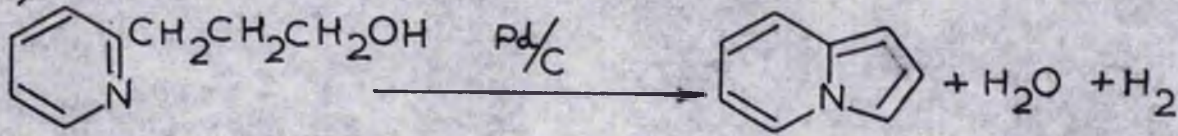
(c) <u>Boekelheide's Synthesis</u>.

A synthetic route which, as yet, is of unknown generality but has so far been employed to prepare the more inaccessible 5-methylindolizine[19] and the parent base,[19,20] together with 5-methyl-2-phenylindolizine,[20] in high yields is that devised by Boekelheide and his school.

The method involves the dehydrogenative cyclisation of 3-(2'-pyridyl)

-1-propanol (10) or its derivatives (11) and (12), with 30% palladium on charcoal catalyst, prepared using formaldehyde; the reaction is carried out by heating in an atmosphere of nitrogen.

(10)



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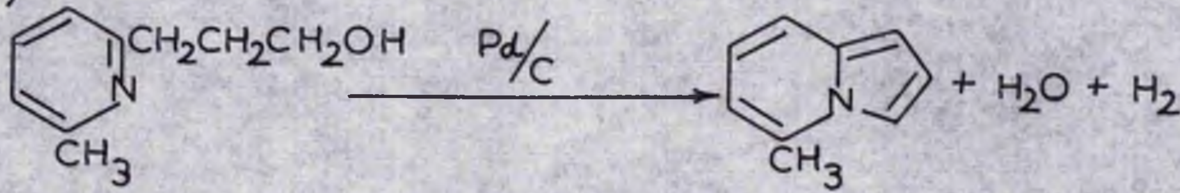

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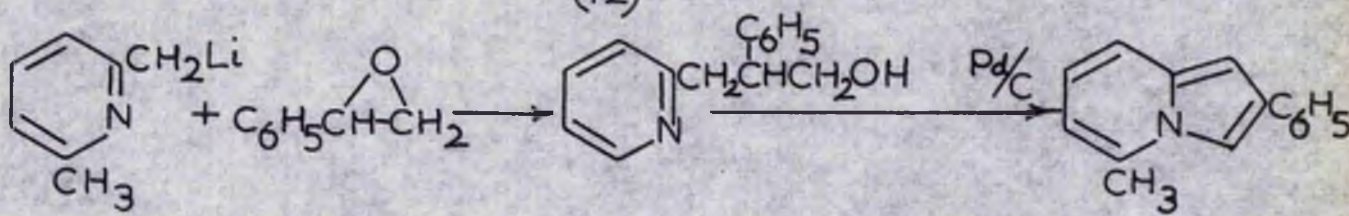
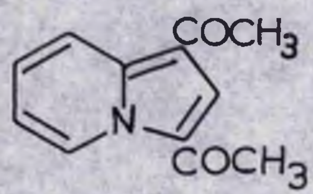


The cyclisation of 3-(2'-pyridyl)-1-propanol has been studied in some detail[19] and there is evidence that the alcohol is initially dehydrogenated to the corresponding 3-(2'-pyridyl)-1-propionaldehyde. The method supersedes Boekelheide's earlier syntheses of indolizine[21] and 5-methyl-indolizine.[20]

(d) Scholtz's Synthesis.

The reaction of acetic and propionic anhydrides with 2-picoline and its derivatives, first utilised by Scholtz in the first synthesis of indolizine by acid hydrolysis of his so called "picolide", later shown to be 1,3-diacetylindolizine[22] (13), is a method of limited generality. However it has the advantage of simplicity and the use of readily available reactants. Tschitschibabin and Stepanov[23] showed that reaction between 2-picoline and propionic anhydride gave (14) and propounded a mechanism accounting for structures (13) and (14). According to this mechanism the first product is the ω-diacetylpicoline (15) which undergoes ring closure through a tautomeric form (16) to 2-hydroxy-1-acetyl-2,3-dihydroindolizine (17). Dehydration and subsequent acetylation of (17) yields (13).

(13)



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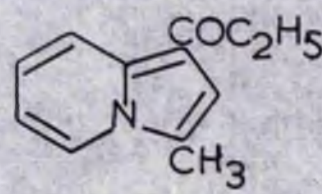

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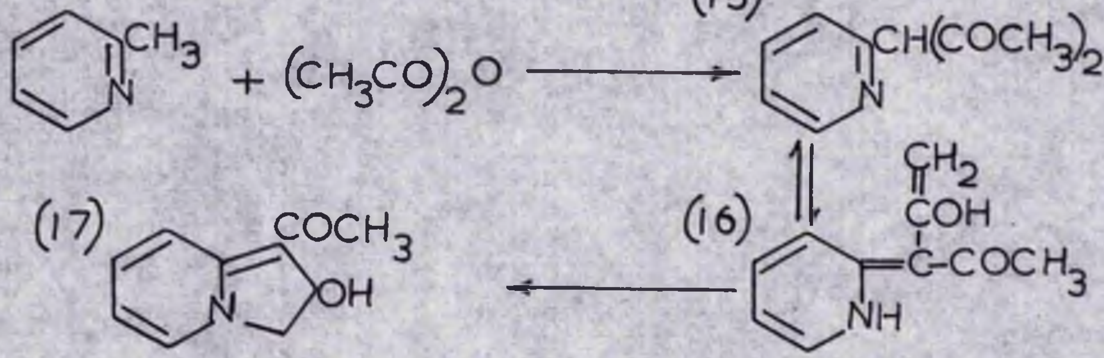

Attempts to extend the reaction to other acid anhydrides,[24] or to condense quinaldine with acetic anhydride, have proved unsuccessful.[12]

(e) Miscellaneous Syntheses.

There have been reported a number of miscellaneous syntheses of little preparative value. These are summarised below in approximate order of importance as synthetic routes to indolizines.

Diels and his collaborators investigated[2,25,26,27,28,29,30] the reaction between dimethyl acetylenedicarboxylate and pyridine and its derivatives. The reaction involves attack on the nitrogen atom. Originally these products were formulated as zwitterionic compounds (18),[26,27,28] but recently they have been shown to be quinolizine derivatives[31] which when suitably treated yielded indolizine derivatives.

Thus when pyridine is treated with dimethyl acetylenedicarboxylate in ether solution, besides the formation of trimethylindolizine-1,2,3-tricarboxylate (22), three other products are isolated; a red labile adduct now formulated as (19), a yellow stable adduct (20),[32,33] and the so called "Kashimoto's compound" now shown to be (21)[31,32]. Treatment of (20)[25] with bromine followed by hydrolysis or oxidation with nitric or chromic acid produced trimethylindolizine-1,2,3-tricarboxylate (22), saponification and partial decarboxylation of which afforded indolizine-2-carboxylic acid. On merely being heated with phenol, formic acid or potassium hydroxide compound (20) rearranges to structure (23)[29,33]. The indolizines (23) and (24) are reported[28] to have been obtained when pyridine reacts with acetylenedicarboxylic ester in methanol, when reaction is carried out with and without cooling, respectively.

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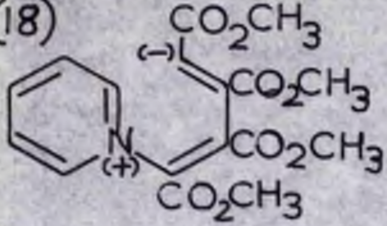

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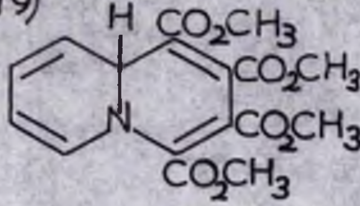

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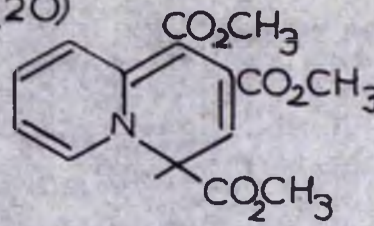

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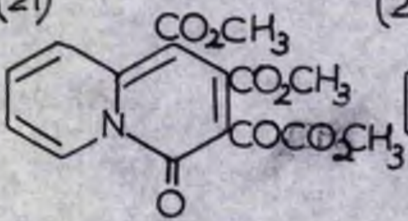

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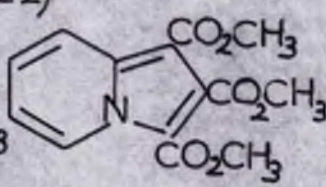

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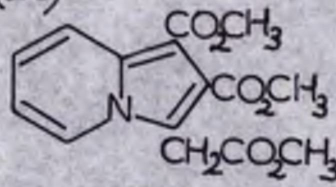

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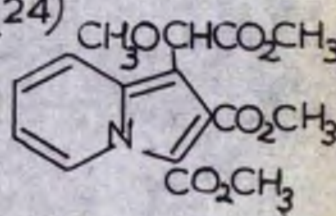
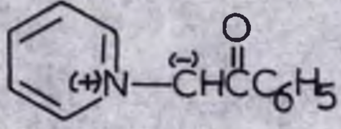


Electrophilic attack of dimethyl acetylene dicarboxylate on the zwitterion (25), derived from the treatment of 1-phenacyl pyridinium bromide with base, and the subsequent cyclisation in the presence of palladium on charcoal catalyst produced **1,2-diacetyl-3-benzoylindolizine** (26)[34] which on hydrolysis and treatment with acid was converted into **indolizine-2-carboxylic acid.**

(25)


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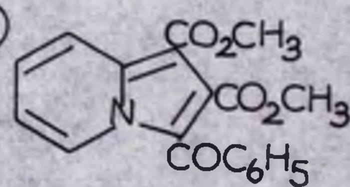
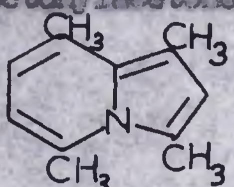


The condensation of 2,4-dimethylpyrrole with acetylacetone, or with itself in acetic acid solution in the presence of zinc acetate yielded[35,36,37] the tetramethylindolizines (27) and (28). A more convenient route to (27) is to condense 2,4-dimethylpyrrole with acetonylacetone in ethanolic hydrogen chloride.[38]

(27)


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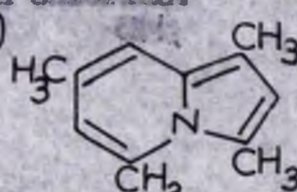
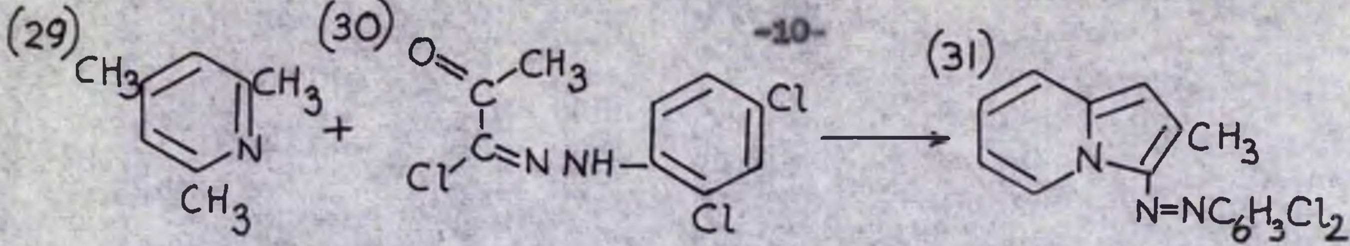
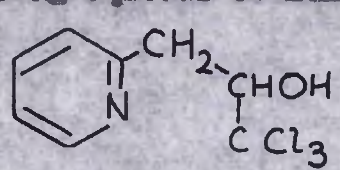


Treatment of collidine (29) withthe chloro compound (30) gave a product for which structure (31)[38] was suggested.



Compound (32) formed by the addition of chloral to 2-picoline was reduced in low yield to (33) which on subsequent treatment with strong aqueous sodium hydroxide produced indolizine.[39]

(32)



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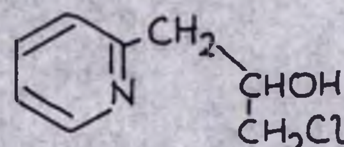
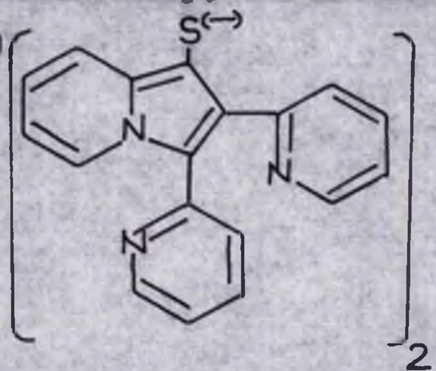


Heating 2-picoline with sulphur produced [40,41] (34) and (35) simultaneously, the latter also being obtained by reduction of (34).

(34)



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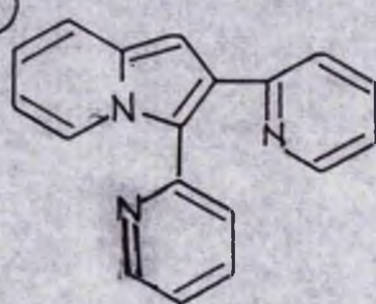


Traces of indolizine[42] are formed along with pyrrole, indole and carbazole, when furan and ammonia are passed over alumina at 400°. Indolizine[43] has also been found among the products of pyrolytic decomposition of pyridine.

XIII Indolizines: Physical Properties.

Indolizine and its simple alkyl derivatives are liquids or low melting solids unstable to light or air, and volatile in steam. This last property is utilised in their preparation and purification. By contrast, the simple 2-aryl substituted indolizines are relatively high melting, stable crystalline solids. 1-Aryl substituted indolizines and their homologues are more usually liquids at room temperature. Many indolizines are fluorescent under ultraviolet light; some fluoresce in daylight. The ultraviolet absorption spectra of numerous indolizines have been recorded. Indolizines are weakly basic and form salts with mineral acids. The base strengths of indolizines and ten of its methyl homologues were determined[44] in 80% ethanol and are tabulated below. The resonance energy of indolizine has been calculated by molecular orbital methods as 82 k.cals[45]/mole. The π-electron densities[46] fig. 5(b), frontier[47,48] electron-densities fig. 5(c) for electrophilic substitution, mobile bond orders,[46] atom localisation energies for electrophilic, radical and nucleophilic reactions[19] at various sites, in addition to bond localisation energies[19] have been calculated.

Indolizine	PKb
Indolizine	11.57
1-Methylindolizine	10.40
2-Methylindolizine	9.87
3-Methylindolizine	11.10
1,2-Dimethylindolizine	8.57

Indolizine	PKb
2,3-Dimethylindolizine	10.40
1,3-Dimethylindolizine	10.80
2,5- " "	9.04
2,6 " "	9.39
2,7 " "	8.74
1,2,3-Trimethylindolizine	9.21

AIV The Relationship of Indolisine to other Aromatic Systems.

AIV_1 Introduction.

Indolisine has until recently been regarded as a derivative of pyrrole and compared with the isoelectronic N heteroaromatic indole[45]. Explicit recognition of, and investigation into, the inherent aromaticity of the indolisine system has only come about in the last fifteen years.

It is true that the chemistry of pyrrole and indole is also largely displayed by indolisine, particularly with respect to the great ease of electrophilic substitution. However, considerations of the mechanism by which these electrophilic substitution reactions proceed lead to a more profound and equally valid analogy to yet another aromatic system, azulene.

To qualify this statement a brief survey of the concept of aromaticity, with passing reference to the aromatic characters of azulene and indole, and concluding with a fuller account of the aromatic character and chemistry of indolisine, would appear to be relevant.

AIV_2 The Concept of Aromaticity.

Organic chemists had for some time classed compounds which were stable, and behaved like benzene in preferably undergoing substitution rather than addition reactions and hence maintaining the system's nucleus, as aromatic.[49] This classification is unfortunate in two respects: (a) As the classification is based on semi-quantitative properties rather than on qualative ones, it is necessary for classification purposes to draw an arbitrary limit on one side of which a compound is classified as aromatic and on the other as nonaromatic. If different criteria were used simultaneously, a compound may be classified as aromatic according to one and as non-aromatic according to another. (b) Classification is possible only after the compound in question has been prepared and its properties have been determined.

A more satisfactory definition based on some qualitative structural feature would be useful as it would permit unambiguous classification. The properties of the compound formally defined as 'aromatic' should then have no bearing on the classification. Thus the modern concept of aromaticity is to be distinguished from aromatic or benzene-like behaviour. Aromaticity is a property of the compound in the ground state whereas aromatic behaviour or reactivity depends on the difference in the free energy between that of the ground state and that of the transition state or intermediate of the chemical change involved. It is true that a compound which exhibits aromatic behaviour also exhibits to a varying degree aromaticity, but a compound which shows aromaticity need not necessarily show aromatic behaviour. An acceptable definition of aromaticity may then be: A structure is aromatic if the atoms are so arranged, so that π-electrons can be delocalised over that structure.

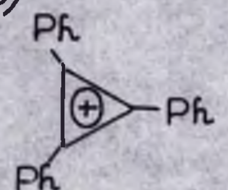
Valid criteria for aromaticity are therefore physical properties of the system rather than its chemical reactivity. The most important of such properties are, (a) a lower energy content than would be predicted by comparison with an appropriate acyclic analogue, viz. resonance energy. (b) The ability of the compound to sustain an induced ring current of π-electrons[50] and (c) the presence of carbon - carbon bonds which are intermediate in length between those usual for single and double bonds.

AIV_5 <u>The application and Validity of Hückel's Rule</u>.

No fundamental understanding for the feasability that a particular cyclic structure containing π-electrons should exhibit aromaticity was realised until the application of simple molecular orbital theory[51,52,53] to such cyclic structures. The generalisation from these calculations is now known as the Hückel rule, whereby aromaticity is predicted to be shown by conjugated monocyclic systems having $(4n+2)\pi$-electrons where n is an integral number.

One of the triumphs of the theory was the isolation and relative stability of the cyclopropenylium cations (36)[54] and (37).[55] Significantly the anion $Ph_3C_3^{(-)}$ [56] and radical Ph_3C_3 [57] corresponding to (36) are not stable.

(36)



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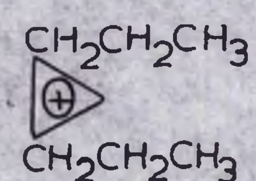


When n = 1, Hückel's rule embraces the 'aromatic sextet'[58] concept of Robinson and predicts that carbocyclic structures with 6π electrons should show aromaticity. Benzene is the foremost example; its properties are well known. The stability is enhanced by the fact that the geometry of the molecule in the planar state, in which delocalisation is most effective, does not necessitate angle strain.

Besides benzene other monocarbocyclic ring systems which contain 6π electrons and should therefore exhibit aromaticity if not aromatic behaviour in their simplest form are the cyclopentadienide anion and the cycloheptatrienylium cation.

The resonance stabilisation of the cyclopentadienide anion is borne out by (a) the acidity of cyclopentadiene[59,60] leading to the formation of salts, (b) the stabilities of cyclopentadiene derivatives having an extracyclic double bond [(38)(a)] and [(38)(b)]. The latter depends on the electronegativity of the exocyclic atom or group X. Where polarisation can develop in the sense [(38)(b)], that structure should be further stabilised. Thus fulvene ((38) X=CH_2) can be isolated as a yellow unstable oil[61] with a dipole moment (1.1D)[62] and moderate resonance energy. These properties indicate the presence of the ylide structure [(38)(b)].

(38)a (38)b

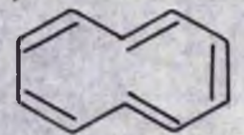
Examples of compounds in which the ylide structure is fully developed are the ionic structures of diazonium,[63] and triphenylphosphonium[64] cyclopentadienylides ((38)b X^{+}= $-N\equiv N$ and $-P\,Ph_3$). The non existance of cyclopentadienone on the other hand, except as a special derivative[65] is attributed to the fact that the ylide structure is impossible, since oxygen is more electronegative than carbon (c.f. the relative stabilities of diphenylcyclopropenone[66] and tropone). (c) The undoubted stability of and aromatic behaviour of cyclopentadienyl iron[67,68,69,70,71] (ferrocene).

Although synthesised probably as early as 1891,[72] the aromaticity associated with the cycloheptatrienylium cation was not recognised until 1954.[73] Significantly, cycloheptatrienone or tropone presents no difficulty in its syntheses,[74] as in this case the normal polarisability of the carbonyl group is complementary to the requirements of the ring for developing an aromatic sextet. This is reflected in its large dipole moment (4.3 D)[75] and abnormally low carbonyl stretching frequency (1638 cm^{-1}).[74]

Only one monocycle with 10 π electrons (n=2) has been prepared, that of the cyclooctatetraenyl dianion[76] (39). The action of alkali metals on cyclooctatetraene in ether or liquid ammonia produces the dianion in equilibrium with a small amount of the radical anion. In tetrahydrofuran the di-salt can be isolated. Evidence for its planarity and associated aromaticity is based on the N.M.R. spectrum

(39)

(40)

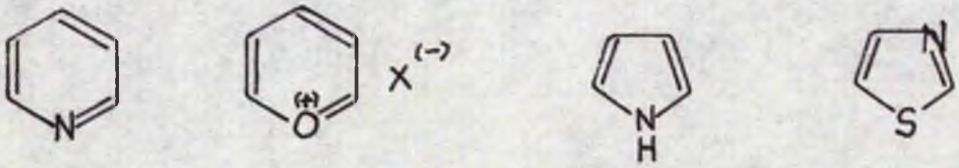


Cyclodecapentaene (40) has not been isolated implying an unstable structure. This apparent failure of Hückel's rule is attributed to the mutual inside steric interference of the hydrogen atoms when a hypothetical planar conformation is constructed for the molecule. The strain in the system (40) may therefore be out of all proportion to the resonance energy which would be developed by the assumption of the planar state. It was predicted[77,78,79] that this effect of steric clash between internal hydrogen atoms would operate prohibiting planar or near planar conformations up to [18]-annulene[79] (cyclooctadecanonaene), which, it was suggested, might show diminished unsaturation characteristic of aromatic compounds, in agreement with Hückel's rule (n=4). The cyclopolyenes [18] -annulene, [24] -annulene and [30] -annulene and a number of other macrocyclic molecules [79,80,81] have recently been prepared. [18] -Annulene was found to be reactive and hydrogenated readily to the cycloalkane. Evidence that the hydrocarbon exhibits aromaticity in the sense of being able to sustain an induced ring current is provided by the N.M.R. spectrum[79] and X-ray structural analysis suggests[79] that the bonds do not alternate in length.

Negative evidence for the validity of Hückel's rule is the non aromaticity of cyclobutadiene and cyclo-octatetraene.

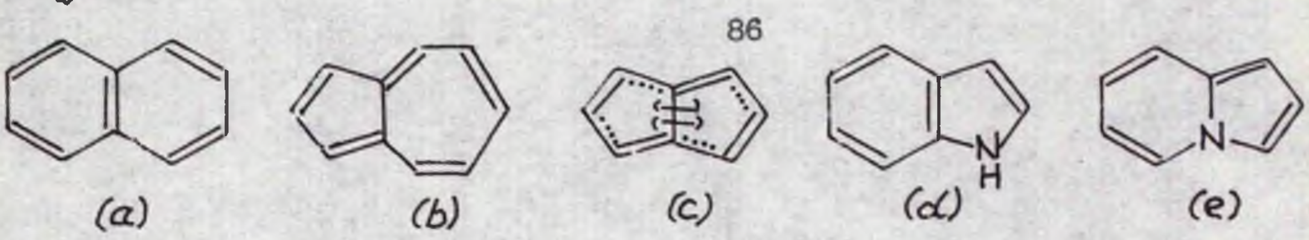
Huckel's rule, strictly applicable to monocarbocycles, can be logically extended to hetero-monocyclic systems, which will be aromatic provided that the number of π- electrons conforms to the pattern (4n+2). Examples of such systems are shown in fig. 1 below:

Fig. 1



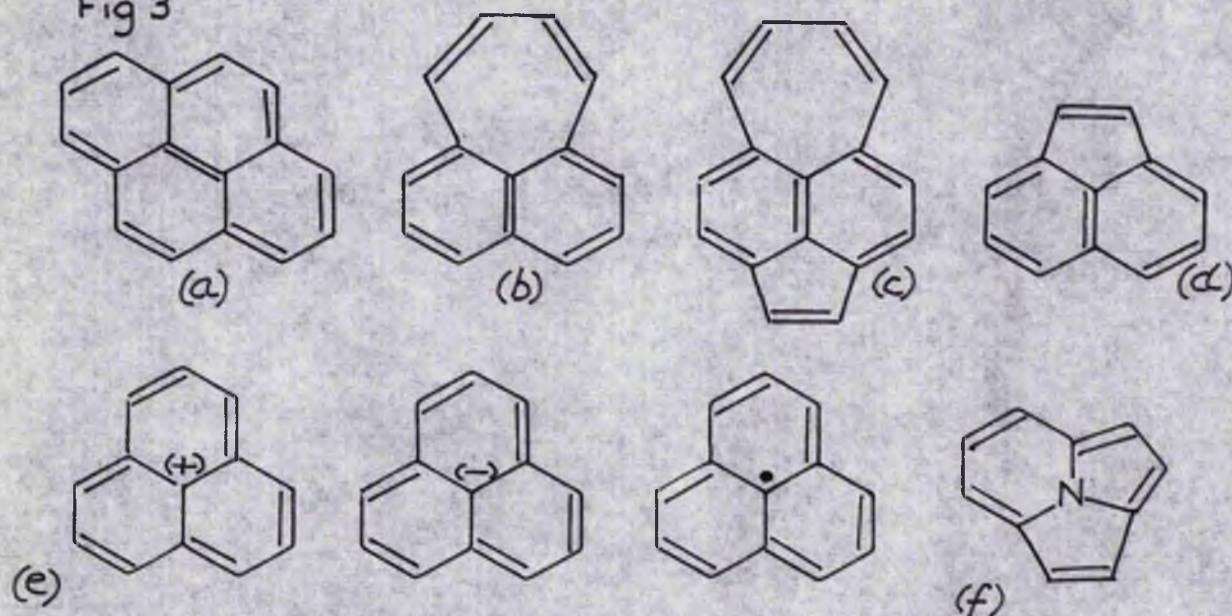
It has also been found applicable to structures in which all the atomic orbitals participating in the π -electron system are peripheral.[82] Thus the examples of 10 π carbobicyclic and hetero-bicyclic systems shown in fig. 2 should also exhibit aromaticity whereas heptalene[83] and pentalene[84,85] should not.

Fig. 2



However, extension of Huckel's rule to polycyclic structures particularly in which there is peri ring fusion such as in (a) pyrene (b) pleiadiene[87] (c) aceplèiadylene[87] (d) acenaphthylene (e) perinaphthenyl cation,[88] anion[89] and[90] radical (f) cyclazine,[19,20,91] shown on fig. 3, is no longer justified. Although application of the 4n+2 rule to the periphery of the molecule and the treatment of cross links as perturbations can be a useful guide to predict aromaticity in such cases. However it is generally more satisfactory with polycyclic systems to carry out a separate molecular orbital calculation on each system.

Fig 3



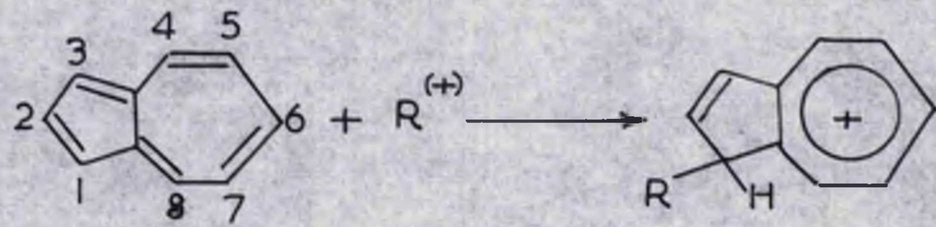
AIV$_4$ <u>The Aromaticity of Azulene.</u>

Azulene fig. 2 (b), in particular, can be considered as a 10 π electron structure in which there is extensive peripheral delocalisation in the ground state, and in which the problem of internal steric interference present in cyclodecapentaene has been obviated by a trans annular valency bridge. Accordingly, the bridging bond is predominantly single bond in character[92] and azulene has a high resonance energy (40 K.cals/mole)[93] It also shows aromatic behaviour in its ability to undergo both electrophilic and nucleophilic substitution reactions.

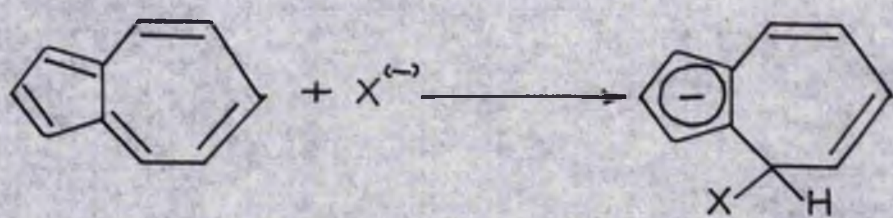
The ease with which azulene undergoes electrophilic and nucleophilic substitution is attributed to the ease with which π-electron sextets may be developed in either ring, depending on the nature of the attacking reagent. During reaction, the transition states are stabilised by the formation of a tropylium cation or cyclopentadienide anion. For this reason the resonance energy difference between the ground state and that of the transition intermediates fig. 4 (a) and (b) will be small and aromatic behaviour or reactivity increased.

Fig. 4

(a) Electrophilic Attack.



(b) Nucleophilic Attack.



The indicated stability of the transition intermediate fig.4 (a) is endorsed by the actual isolation of azulenium salts.[94] The predicted formation of the 1H azulenium cation when azulene was treated with acids[95,96] was previously confirmed by a proton magnetic resonance[97] study of azulene when dissolved in trifluoroacetic acid.

AIV$_5$ The aromaticity of Indole.

If resonance energy is taken as a guide to aromaticity then the resonance energy of indole (47-54 K.cals/mole)[98,99] compares with that of azulene. However, as in the case of azulene indole displays its aromatic character through its reactivity in substitution reactions.

In indole fig. 2 (d) the π electrons, one contributed from each of the eight carbon atoms and two from the nitrogen atom, probably do not participate so completely in peripheral delocalisation, since the bond order of the bridging bond is not the lowest in the molecule. It is however the lowest bond order of all the bonds constituting the six membered ring.[46]

Although the hetero atom gains the largest share in the two electrons it contributes to the ten π electrons delocalised over the nine atomic centres, all the carbon centres have electron densities greater than one.[47] Thus indole would be expected to react only with electrophilic reagents. Electron density calculations suggest that electrophilic reagents should attack and under non reversible conditions substitute, firstly at the hetero atom, then at position 3, followed by position 2. These interpretations are largely borne out in the chemistry of indole.

It may be significant that as yet no indolium salts have been isolated, although positions of protonation have been investigated.[100] Indole and its derivatives readily dimerise when treated with acids.[101] Thus although indole readily undergoes electrophilic substitution it would seem that it does so more by virtue of its higher electron density at the position of attack than the ability of its structure to accommodate a particularly stable transition intermediate. No postulated transition intermediate of indole can incorporate the positive charge acquired during electrophilic attack, to give a recognised cationic structure containing six π-electrons in a ring.

These notions can be expressed in thermodynamic and kinetic terms. According to the transition state theory

$$k_r = \frac{kT}{h} e^{\Delta S^{\#}/R} e^{-\Delta H^{\#}/RT}$$

where h - Planck's constant

R - gas constant

k - Boltzmann constant

T - degrees Kelvin

$\Delta S^{\#}$ - entropy of activation

$\Delta H^{\#}$ - enthalpy of activation

Thus the rate constant k_r for a given reaction at a fixed temperature depends on two factors.

(a) The enthalpy of activation $\Delta H^{\#}$. This is equivalent to the difference in resonance energy between transition and ground states.

(b) The entropy change $\Delta S^{\#}$ of the system in the process of changing from the ground to the transition state.

It is suggested that for a given reaction between an electrophile R^+ and the two systems azulene and indole, reaction with azulene should be facilitated compared with indole on account of factor (a). Reaction with indole should be facilitated compared with azulene on account of factor (b), due to the higher electron density on the nitrogen atom (indole 1.74; for azulene 1.17[102] at C_1). Thus there is the possibility of greater charge neutralisation by attack on the indole molecule i.e. the possibility of greater entropy change.

If the reaction is reversible then factor (a) is operative and the transition state with the greatest possibilities for delocalisation of the residual π-electrons and the acquired positive charge, is adopted . In indole it would appear that the weaker carbon - nitrogen[105] bond renders the reaction reversible, and 3-substitution is promoted under more vigorous conditions, thus implying that a δ-transition intermediate of greater resonance stability is gained through 3-substitution.

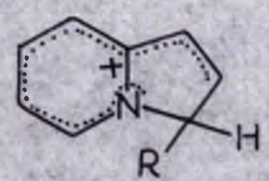
AIV$_6$ The Aromaticity of Indolisine.

As in indole, so too, in indolisine each of the eight carbon atoms contribute one π- electron and the nitrogen atom two, to give a total of 10 π electrons delocalised over nine atomic centres. That these electrons participate in peripheral delocalisation, in the ground state, is indicated from the calculated bond orders, the bond common to the two rings having the lowest order[46] fig. 5 (a).

The greater electronegativity of the nitrogen atom ensures that it has a predominant share in the two π-electrons it contributes to the peripheral dectet. The calculated electron densities are shown in fig. 5 (b). The calculated frontier electron densities for electrophilic substitution are shown in fig. 5 (c). The important difference between fig. 5 (b) and fig. 5 (c) is the promotion of sites 3 and 1 in fig. 5 (c) to positions of higher electron density over that of the nitrogen atom. This is in agreement with experimental observations.

anticipated that the system should be susceptible to electrophilic substitution. A transition state of type shown in fig. 6 (a) may be visualised, in which the positive charge acquired from the attacking electrophile R^+, is spread over the residual eight centres. However, as in the case of azulene, the electrons can regroup[104] themselves, and the positive charge absorbed to give the stable pyridinium sextet, as illustrated in the postulated transition intermediate fig. 6 (b)

Fig.6

(a) 

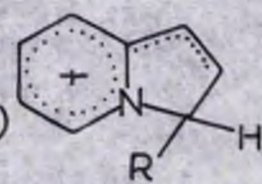
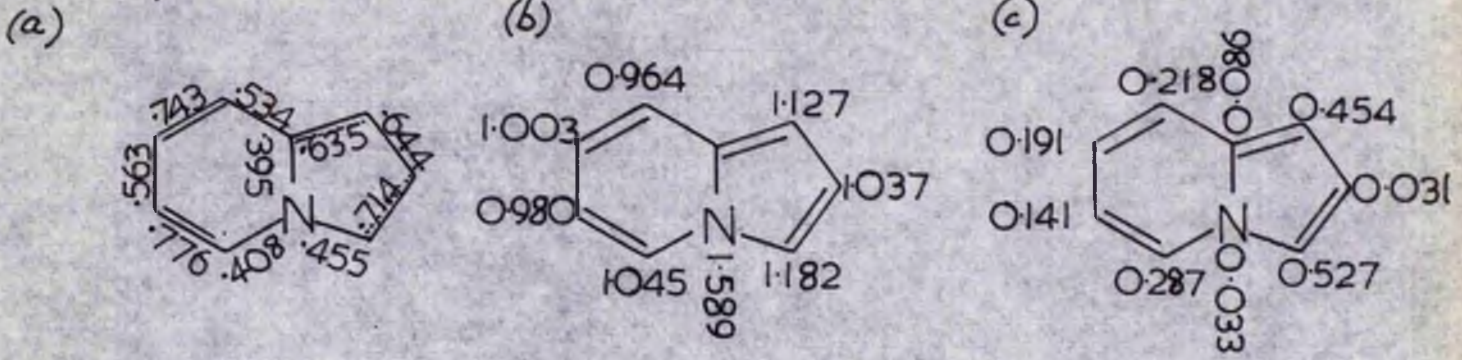
(b) 

Fig. (5)

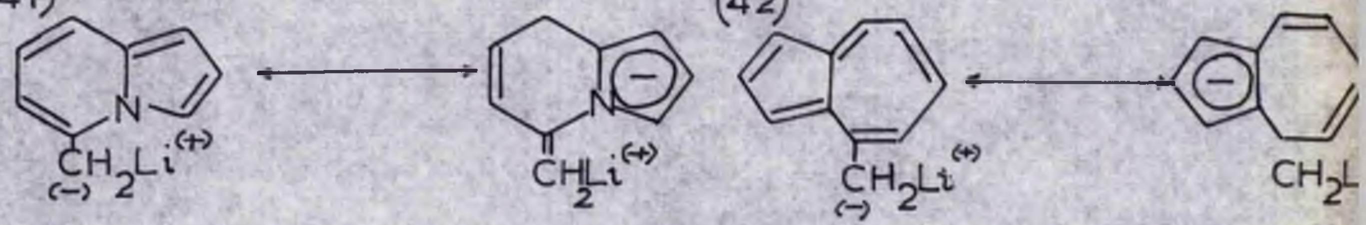


By analogy of indolizine to indole alone therefore, it may be

The isolation in many instances, CII, of stable indolizinium salts may give a guide as to the stability of the Δ transition intermediate fig.6 (b) and could largely account for the ease with which indolizines undergo electrophilic substitution and replacement reactions. Facilitated electrophilic attack at the reactive 3 and to a lesser extent 1-position would also be anticipated from the high electron density values of those sites, although these values are lower than that of the 1-position of indole. Thus indolizine should show as great if not a greater reactivity to electrophilic reagents than either azulene or indole. This inference is largely confirmed in the electrophilic substitution reactions of indolizine which are discussed in section AV.

From fig. 5 (b), since no carbon atom has an abnormally low electron density and since no transition intermediate containing a particularly stable anionic structure can be developed, nucleophilic attack of indolizine would not be expected to occur readily. The predicted sites of attack according to fig. 5 (b) are the six and eight positions, whereas atom localisation energy calculations for both nucleophilic, and incidentally radical attack, predict the five or eight positions.[19] The sole attempt to subject indolizine to nucleophilic substitution (treatment with sodamide)[18] was unsuccessful. However it has been shown that the hydrogen atoms of 5-methylindolizines are acidic[91,20] and replaceable with metal atoms. Thus the anion (41) formed by proton loss in 5-methylindolizine when treated with n-butyllithium is similar to those formed by the action of bases (PhNMeLi^{+}) on 4(8)-methyl-azulenes,[106] (42).

(41) (42)



All three systems viz. azulene, indole and indolizine, show olefinic character in their behaviour towards oxidising and reducing agents. This is due to the lack of uniformity of the field in which the π-electrons move so that the electronic charge in the ground state is permanently displaced from one electron per atomic centre, giving rise to variable bond orders. The bonds with the greatest olefinic character are then susceptible to oxidation or reduction. Thus indolizine and its simple alkyl derivatives are attacked[1,107] by potassium permanganate, chromic acid, peracetic acid,[4,6,10,11,12,107,108], and even atmospheric oxygen. Indolizine resists reduction by zinc and acid[1] and hydrogenation over a palladium-charcoal catalyst.[12] Hydrogenation to 5,6,7,8 - tetrahydroindolizine is effected using Raney nickel or Adam's catalyst at low temperature.[4] The use of higher temperatures results in the reduction to the octahydro compounds. Hydrogenation of indolizine in the presence of strong acid however, yields 3H-1,2-dihydroindolizine.[109]

IV Electrophilic Substitution Reactions.

IV$_1$ Introduction.

It was anticipated from the previous section that electrophilic substitution should occur at the 3-position using mild reagents and conditions. That this is so is exemplified by reference to the more common electrophilic reagents. Evidence for substitution at position 3, or exceptionally position 1 in the case of nitration, has been specifically determined for electrophilic reactions on 2-methyl and in some cases 2-phenylindolizine, and analogous behaviour is generally inferred in the case of other indolizines.

IV$_2$ Acylation

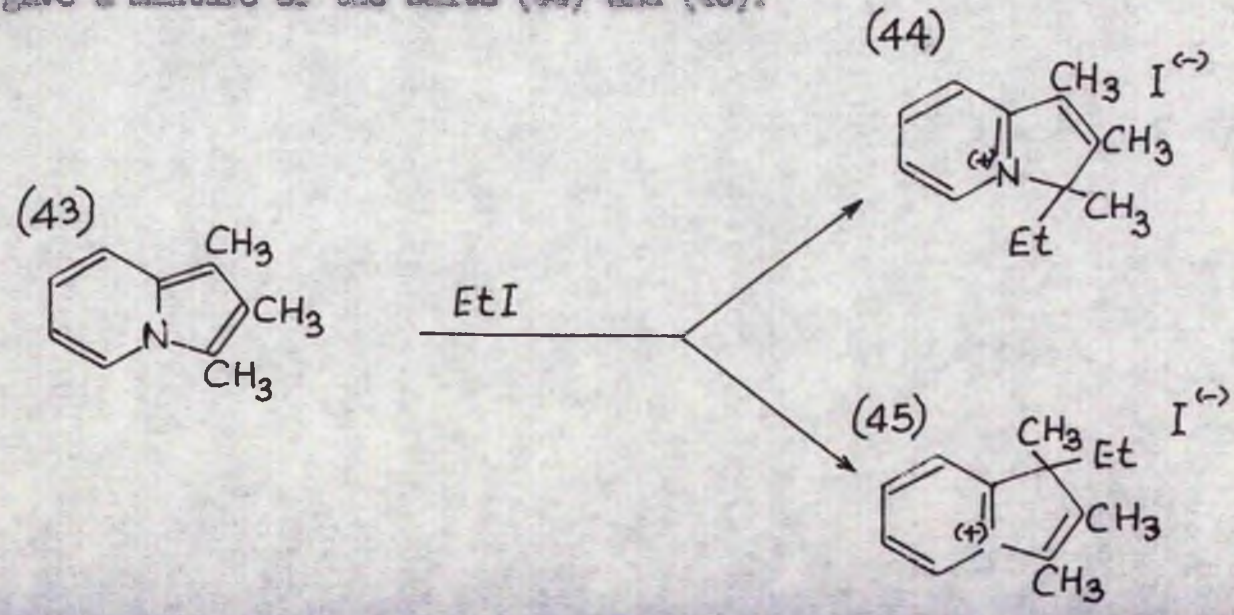
The indolizine nucleus can be readily acetylated merely by heating with an acid anhydride in the presence of the sodium salt of the corresponding acid.[6,22,106,108,110,111.] 3-Monoacetyl or monobenzoyl derivatives are obtained. Higher temperatures and excess acetic anhydride produces the 1,3-diacetyl compounds[6,22] whereas the action of benzoyl chloride in the cold gives the monobenzoyl derivative.[6,24,111] In contrast both acetyl chloride and acetyl bromide require catalyst to promote substitution.[13]

The acyl group is readily removed by hydrolysis with mineral acid[1,6,16,17,22,25,106] and in the case of 3-acetyl-2-phenylindolizine even 80% acetic acid.[6] Resistance to hydrolysis increases if electron attracting acyl,[6] nitro,[108] or nitroso[11] groups are present in the nucleus. Replacement of the acetyl group by iodine[107] or the nitro[108] group has been reported.

Proof that acetylation occurs preferentially at the 3-position has been shown by reduction of the monoacetyl derivatives of 2-methyl- and 2-phenylindolizines to the 3-ethyl derivatives and comparison with the compounds prepared by direct synthesis. Proof that benzoylation of 2-phenylindolizine also occurs at the 3-position has been established in a similar fashion.[4] The reduction of the acyl groups was effected by a modification of the Clemmensen method for 3-acetyl-2-methylindolizine, a mixture of the required 3-ethyl derivatives and 3-(1-hydroxyethyl)-2-methylindolizine being formed, and by Kon's modification of the Kishner-Wolff method for 3-acetyl and 3-benzoyl-2-phenylindolizines.[4] A superior method for deoxygenation of the keto group is to use lithium aluminium hydride.[111]

IV_3 Alkylation.

Nuclear alkylation also proceeds readily without the aid of a catalyst.[1,106,112] For example 2-methylindolizine when heated with methyl iodide yields first 2,3-dimethyl-, and then 1,2,3-trimethylindolizine (43),[112] which on treatment with ethyl iodide gave a mixture of the salts (44) and (45).[5]



AV_4 Formylation.

Introduction of a formyl group into the indolizine nucleus is readily achieved by the Vilsmaier reaction[111,112,113] using phosphorus oxychloride and N-methylformanilide or dimethylformamide. Formylation occurs preferentially at the 3-position. 1,3-Diformylation by this method has also been reported.[113] A higher yield of 3-formyl-2-methylindolizine is obtained by McFayden-Stevens reduction of 2-methylindolizinyl-3-benzenesulphonylcarbohydrazide[113] whereas under the conditions of the Reimer-Tieman reaction 2-methylindolizine yielded 1,3-diformyl-2-methylindolizine.[112]

AV_5 Halogenation.

Indolizine reacts with bromine or iodine to yield unstable uncharacterisable compounds.[24] Unstable products containing two or four bromine atoms also result from the action of bromine on 1,3-diacetylindolizine in chloroform solution.[1]

AV_6 Aryldiazotisation.

Diazonium coupling occurs preferentially at the 3-position of indolizine[7,8] and its 2-substituted homologues. Blockage of the 3-position directs the attacking group to the 1-position, as indicated by the formation of 3-acetyl-2-methyl-1-phenylazoindolizine which undergoes catalytic reduction to 1-amino-3-acetyl-2-methylindolizine.[114]

AV_7 Nitrosation.

Nuclear nitrosation of indolizine is readily effected by the action of sodium nitrite in acid solution.[11,114,115,116,117].

The 3-nitroso compound is preferentially formed and the 1-nitroso compound only when the 3-position is blocked. Thus 2-phenyl and 2-methylindolizine gave 3-nitroso-2-phenylindolizine and 2-methyl-3-nitrosoindolizine respectively, while 3-acetyl-2-methylindolizine gave 3-acetyl-2-methyl-1-nitrosoindolizine.[11] It is found that these nitroso groups are not readily replaced or hydrolysed.[11] Careful oxidation with peracetic acid, or treatment with nitric acid converts nitrosoindolizines into the corresponding nitro analogues.[11,108]

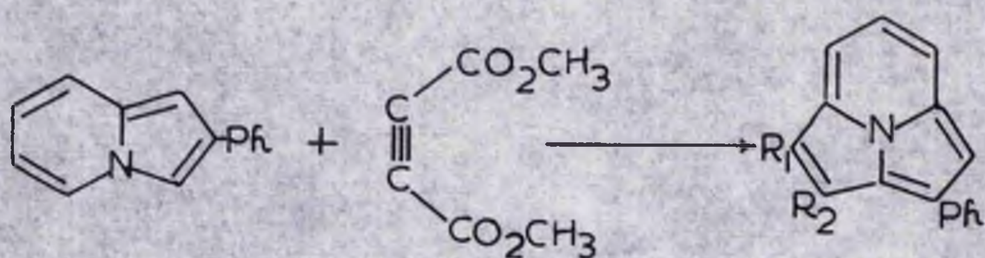
AV$_8$ Nitration.

Indolizine and its 2-homologues are susceptible to oxidation when treated with nitric acid at moderate temperatures for prolonged periods.[108] However by nitrating in sulphuric acid at low temperatures or in the absence of sulphuric acid at high temperatures for a short period, oxidation is minimised and nitroindolizines obtained.[108]

Exceptionally the nitro group preferentially substitutes into the indolizine molecule at the 1-position. Thus both 2-methyl and 2-phenylindolizine gave a large preponderance of the corresponding 1-nitro compounds. With two molecular proportions of nitric acid, 2-phenylindolizine gave exclusively 1-nitro-2-(4-nitrophenyl)indolizine. A further indication of preferential 1-substitution is that a considerably higher yield of 2-methyl-1,3-dinitroindolizine is obtained by nitration of 2-methyl-3-nitroindolizine than by nitration of 2-methyl-1-nitroindolizine,[15] in sulphuric acid.

IV 9 The Reaction of Dimethyl Acetylenedicarboxylate.

Final emphasis of the vulnerability of the indolizine nucleus to electrophilic attack is shown by the reaction of indolizines with dimethyl acetylenedicarboxylate[18] which, contrary to calculations[19] and the usual characteristic of Diels-Alder addition,[118] does not add across the 5- and 8-positions in the six membered ring. Instead, 1,3-dipolar addition occurs at positions 3 and 5, giving cyclazines. Thus the reaction of 2-phenylindolizine with dimethyl acetylenedicarboxylate[34] proceeds smoothly in the presence of 5% palladium on charcoal catalyst to give the corresponding cycl (3.2.2) azine derivative (46) hydrolysis of which gave the dibasic acid (47) which on decarboxylation yields 2-phenylcycl (3.2.2) azine (48). The reaction of indolizine with dimethyl acetylenedicarboxylate has been studied in some detail.[19]



(46) $R_1=R_2=CO_2C$
(47) $R_1=R_2=CO_2$
(48) $R_1=R_2=H$.

The present work has further elucidated the susceptibility of indolizine to electrophilic attack, and its close relationship to azulene, especially in respect of the ease of salt formation during which the pyridinium moiety is developed within the indolizine nucleus.

Protonation, the simplest form of electrophilic attack has been studied in some detail by the use of N.M.R. technique. The reaction of indolizine with a number of other electrophilic reagents, under mild conditions, have been investigated and are discussed in Part B.

PART B

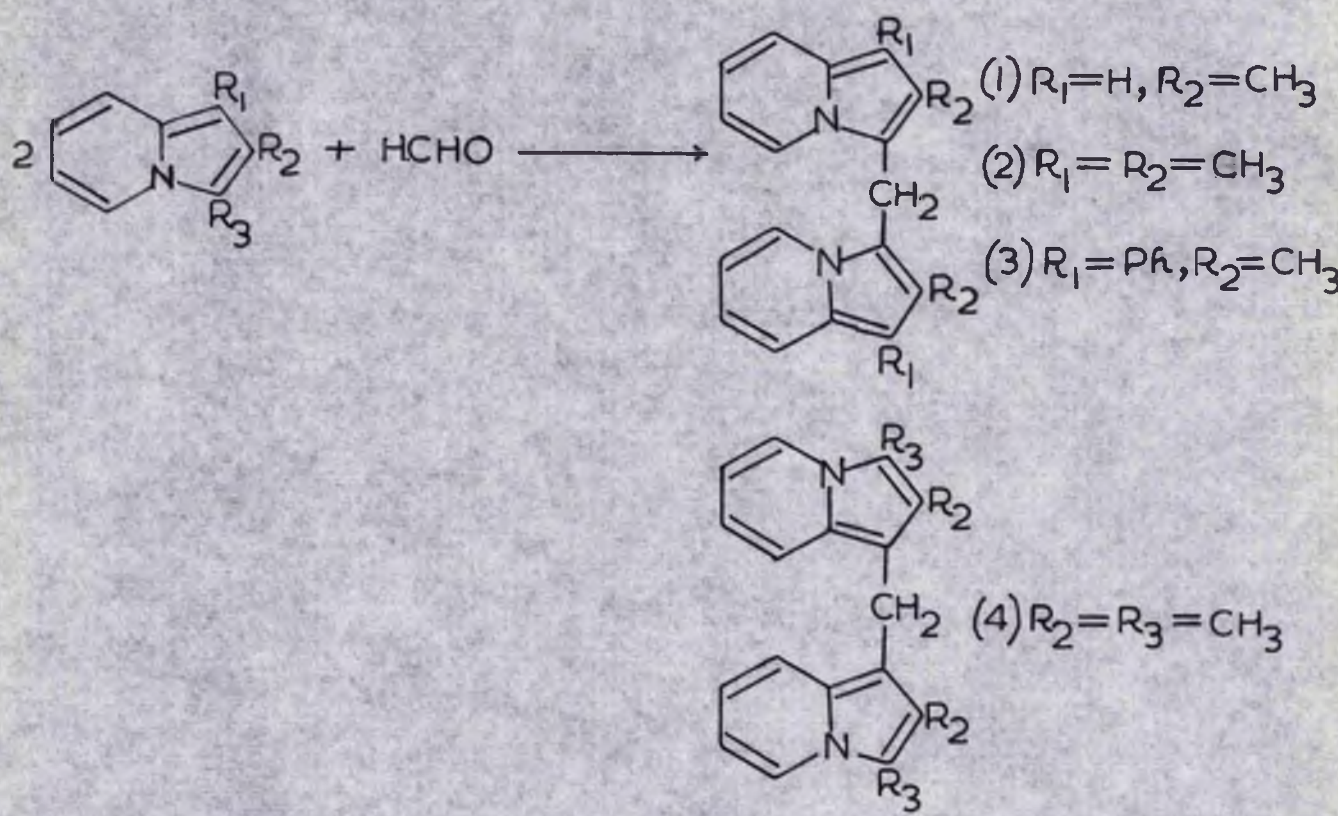
BI Preparation of Indolizines and Di-indolizinylmethanes.

BI$_1$ Preparation of Indolizines.

The following known indolizines were prepared for study: (i) indolizine (ii) 2-methylindolizine (iii) 1,2-dimethylindolizine (iv) 2,3-dimethylindolizine (v) 3-ethyl-2-methylindolizine (vi) 1,2,3-trimethylindolizine (vii) 2-phenylindolizine (viii) 2-methyl-1-phenyl-indolizine (ix) 3-methyl-2-phenylindolizine (x) benzo (g) indolizine. With the exception of indolizine and benzo (g) indolizine, which were prepared by syntheses devised by Boekelheide and his co-workers, the other eight indolizines were prepared by the Tschitschibabin synthesis. 2,3-Dimethylindolizine was also prepared by the lithium aluminium hydride-aluminium chloride reduction of 3-formyl-2-methylindolizine to give an improved yield of 26% as compared to a 10% yield reported by Rossiter and Saxton for the lithium aluminium hydride reduction. The Tschitschibabin method was also employed for the preparation of the following new indolizines: (xi) 2,6-dimethylindolizine (xii) 2,8-dimethylindolizine (xiii) 1-methyl-2-phenylindolizine (xiv) 3-methyl-2-phenylindolizine(xv) 1,3-dimethyl-2-phenylindolizine. The crude indolizines were obtained by standard procedures and were purified in the case of indolizine and its simple alkyl derivatives by distillation under reduced pressure. The more stable arylindolizines were generally purified by recrystallisation.

BI$_2$ Preparation of Di-indolizinylmethanes.

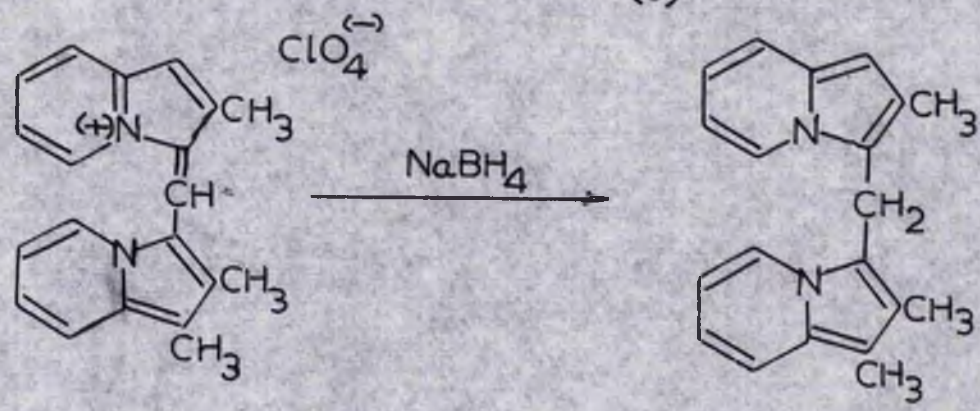
The symmetrical di-indolizinylmethanes (1),(2),(3), and (4) were conveniently prepared by the method of Holland and Naylor[111] in which an ethanolic solution of the indolizine is condensed with formaldehyde.



Sodium borohydride reduction of 3-[2-methylindolizin-3-yl] methylene-1,2-dimethylindolizinium perchlorate (5) in methanol gave the corresponding unsymmetrical methane (6). Depending on the monomethine dye salt reduced, symmetrical and unsymmetrical methanes could be prepared by this method. The ease of this reduction is ascribed to the high positive charge density on the methine carbon atom of the monomethine dye salt (see fig. 4 (13)c).

(5)

(6)



Both methods gave clean nicely crystalline methanes as products whose stability increased with the number of alkyl or aryl substituents added.

BIII Indolizinium Perchlorates.

BIII$_1$ Preparation of Indolizinium Perchlorates.

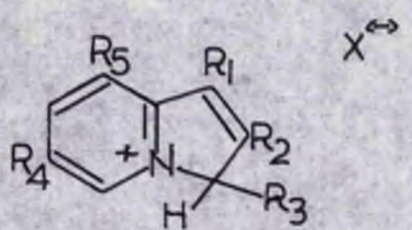
Indolizines react reversibly with acids to form in most cases colourless, stable salts from which the bases are easily regenerated on treatment with alkali. Previous methods[8,112,119] for the formation of indolizinium perchlorates involved the addition of perchloric acid to a methanolic or hydrochloric acid solution of the indolizine or by direct addition of perchloric acid to the base followed by evaporation. The perchlorates of all the above mentioned indolizines were conveniently prepared by the action of 70% perchloric acid on an ethanolic solution of the base. The preparation of the less stable indolizinium perchlorates resulting from the less basic indolizines (indolizine, 2,3-dimethylindolizine, 2-phenylindolizine and benzo (e) indolizine) were carried out in methanol or acetonitrile. The nicely crystalline perchlorates were obtained in yields in excess of 88%, and more generally in excess of 95%, with the exception of benzo (e) indolizinium perchlorate.

BIII$_2$ Introduction to Proton Magnetic Resonance Studies on various Indolizinium Perchlorates.

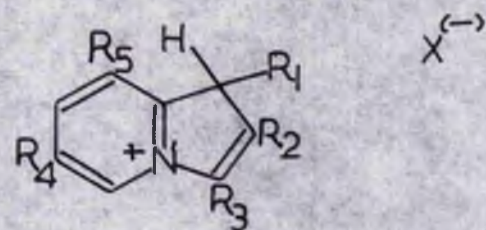
Electrophilic substitution reactions on the indolizine nucleus, discussed briefly in Part A, has been shown to occur exclusively at the 1-or 3-positions, of which the 3-position has proved to be the more reactive. These experimental findings agree generally with theoretical calculations which attribute the highest charge density to the hetero atom or the 1- and 3- positions. Electrophilic substitution is predicted to occur at either the 3- or 1- positions. The former is supported by molecular orbital calculations and the latter by the L.C.A.O. molecular orbital procedure.

Protonation regarded as an electrophilic process would be expected to occur at C-1, C-3, or at nitrogen. Rossiter and Saxton[112] consider that the indolizinium cations result from protonation at the 1- or 3- positions, since such cationic structures contain a true pyridine ring. The selective catalytic hydrogenation of indolizinium bromide[109] (7A (a) X=Br) in the five membered ring to give 5H-1,2-dihydroindolizine was considered to strengthen this viewpoint. The proton magnetic resonance spectra of various indolizinium perchlorates (7(a-1)X=ClO_4) were examined in trifluoracetic acid (10% $^{W}/_{V}$ solutions) in order to determine the preferred position of protonation in these salts.

7A



7B



	Structure Reference	R_1	R_2	R_3	R_4	R_5
(a)	A	H	H	H	H	H
(b)	A	H	Me	H	H	H
(c)	A	Me	Me	H	H	H

Structure	Reference	R_1	R_2	R_3	R_4	R_5
(d)	A	Me	Me	Me	H	H
(e)	A	H	Me	H	Me	H
(f)	A	H	Me	H	H	Me
(g)	A	H	Me	Me	H	H
	B	H	Me	Me	H	H
(h)	A	H	Me	Et	H	H
(i)	A	H	Ph	H	H	H
(j)	A	Me	Ph	H	H	H
(k)	A	H	Ph	Me	H	H
	B	H	Ph	Me	H	H
(l)	A	Me	Ph	Me	H	H
(m)	A	CPh_3	Me	H	H	H

None of the spectra of the indolizinium perchlorates ($7A/_B$(a-l)) shows a broad band or triplet which would arise from a proton bonded to nitrogen. Protonation on carbon must therefore occur with the formation of a methylene or substituted methylene group. The site of protonation was determined by studying the effect of substitution in the five membered ring on the occurance of signals and their multiplicity due to spin - spin coupling.

BII$_5$ Interpretation of the Proton Magnetic Resonance Spectra of Salts 7 (a-l)

TABLE I. Chemical shifts on the δ-scale[120] of the proton magnetic resonance spectra of the indolizinium perchlorates

($7A/_B$ a-1). (Solutions in trifluoroacetic acid. J values refer to protons unless otherwise stated and are in c./sec.).

Proton Signals

Perchlorate	Five-membered ring			Six membered ring			
	H-1	H-2	H-3	H-5	H-6	H-7	H-8
a)$_A$	7.10d J(1,2) 6	7.61d J(2,1) 6	5.55	8.98d J(5,6) 6.5	7.84t	8.47t	8.04d J(8,7) 7.5
b)$_A$	6.85		5.40	8.84d J(5,6) 6.5	7.67t	8.37t	7.85d J(8,7) 8
c)$_A$			5.32	8.85d J(5,6) 6.5	7.78t	8.43t	7.84d J(8,7) 7.5
d)$_A$			5.30 J(H-3 Me-5)=7	8.89d J(5,6) 6.5	7.74t	8.42t	7.86d J(8,7) 8
e)$_A$	6.85		5.41	8.75		8.26d J(7,8) 8.5	7.85d J(8,7) 8.5

Table I (continued)

Proton Signals

Perchlorate	Five membered ring			Six membered ring			
	H-1	H-2	H-3	H-5	H-6	H-7	H-8
f)$_A$	6.95		5.46	8.73d J(5,6) 6.8	7.64q J(65) 6.5 J(6,7) 8	8.33d J(7,6) 8	
g)$_A$	6.82		5.59q J(H-3 Me-3)=7	← complex →			
g)$_B$	4.13			← complex →			
h)$_A$	6.94		5.66 J(H-3 CH_2-3)=3.3	8.87d J(5,6) 6.5	7.85t	8.40t	7.96d J(8,7) 6.5
i)$_A$	7.15		5.87	8.91d J5,6) 6.5		8.40t	7.96d
j)$_A$			5.90	8.92d J(5,6) 6.5		8.47t	
k)$_A$	7.30		6.10q J(H-3 Me-3)=7.5	8.93d J(5,6) 6		8.45t	

Table I (continued)

Proton Signals

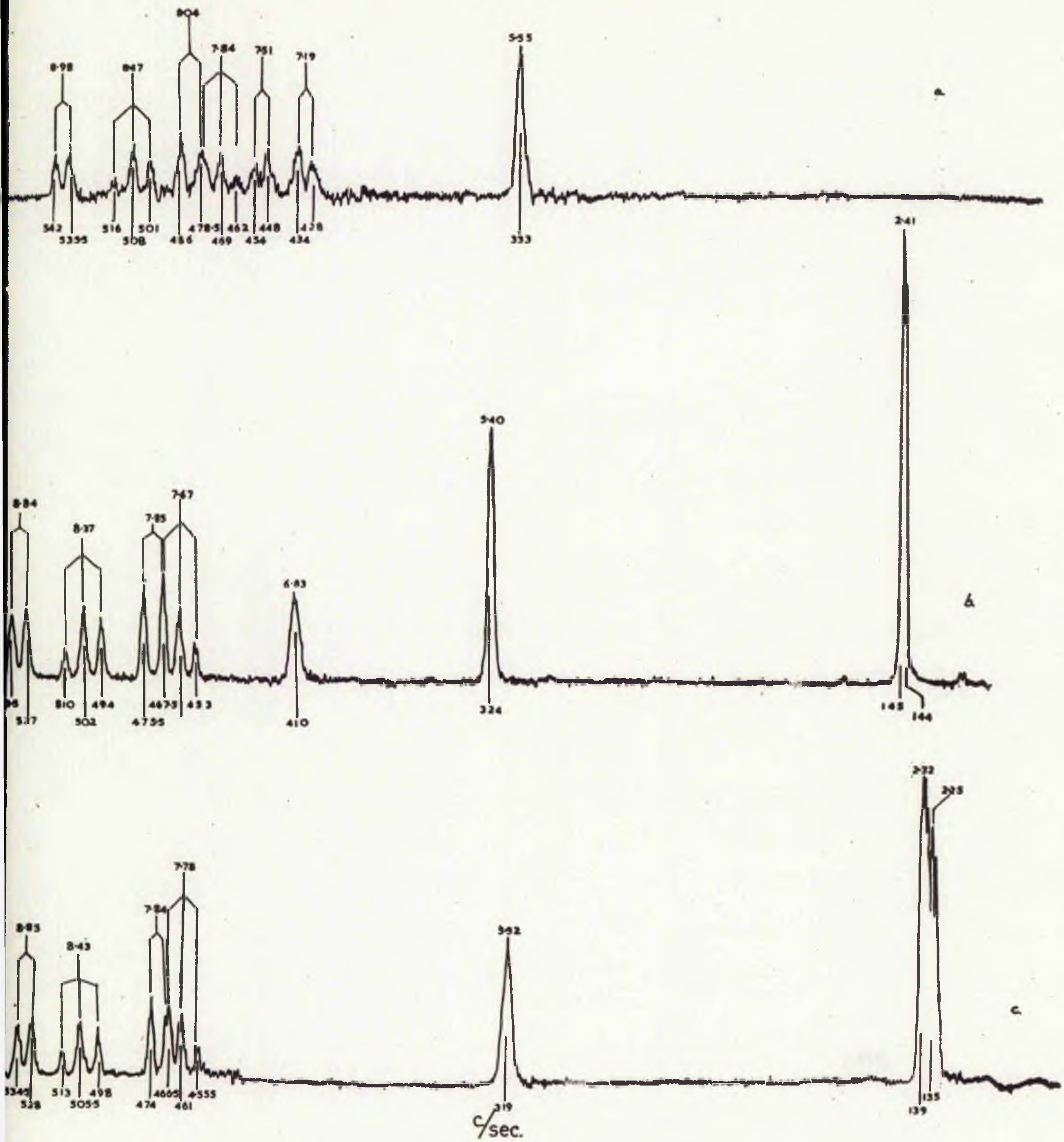
Perchlorate	Five membered ring			Six membered ring			
	H-1	H-2	H-3	H-5	H-6	H-7	H-8
k)$_B$	4.54q						
l)$_A$			5.97q J(H-3 Me-3)=7	8.97d J(5,6) 6.5		8.35t	
m)$_A$			5.65	8.95d J(5,6) 6			

Table I (continued)

Perchlorate	Substituents.				
	1Me	2Me	3Me	6Me	8Me
a)$_A$					
b)$_A$		2.41d J(Me-2 H-1)=1			
c)$_A$	2.25m*	2.32m*			
d)$_A$	2.37	2.27	1.81d J(Me-3 H-3)=7		

Table I (continued)

Perchlorate	Substituents.				
	1Me	2Me	3Me	6Me	8Me
e)$_A$		2.45		2.59	
f)$_A$		2.46d J(Me-2 H-1) 1			2.67
g)$_A$		2.37d	1.66d J(Me-3 H-3)=7		
g)$_B$		2.29	2.43		
				$3\text{-}CH_2\text{-}CH_3$	2-Ph
h)$_A$		2.40		complex 1.57t J(CH_3-CH_2)=8	
i)$_A$					7.52
j)$_A$	2.4t				7.52
k)$_A$			1.69d J(Me-3 H-1)=7		7.55
k)$_B$			2.69t		



a.
b.
c.
c/sec.

Table I (continued)

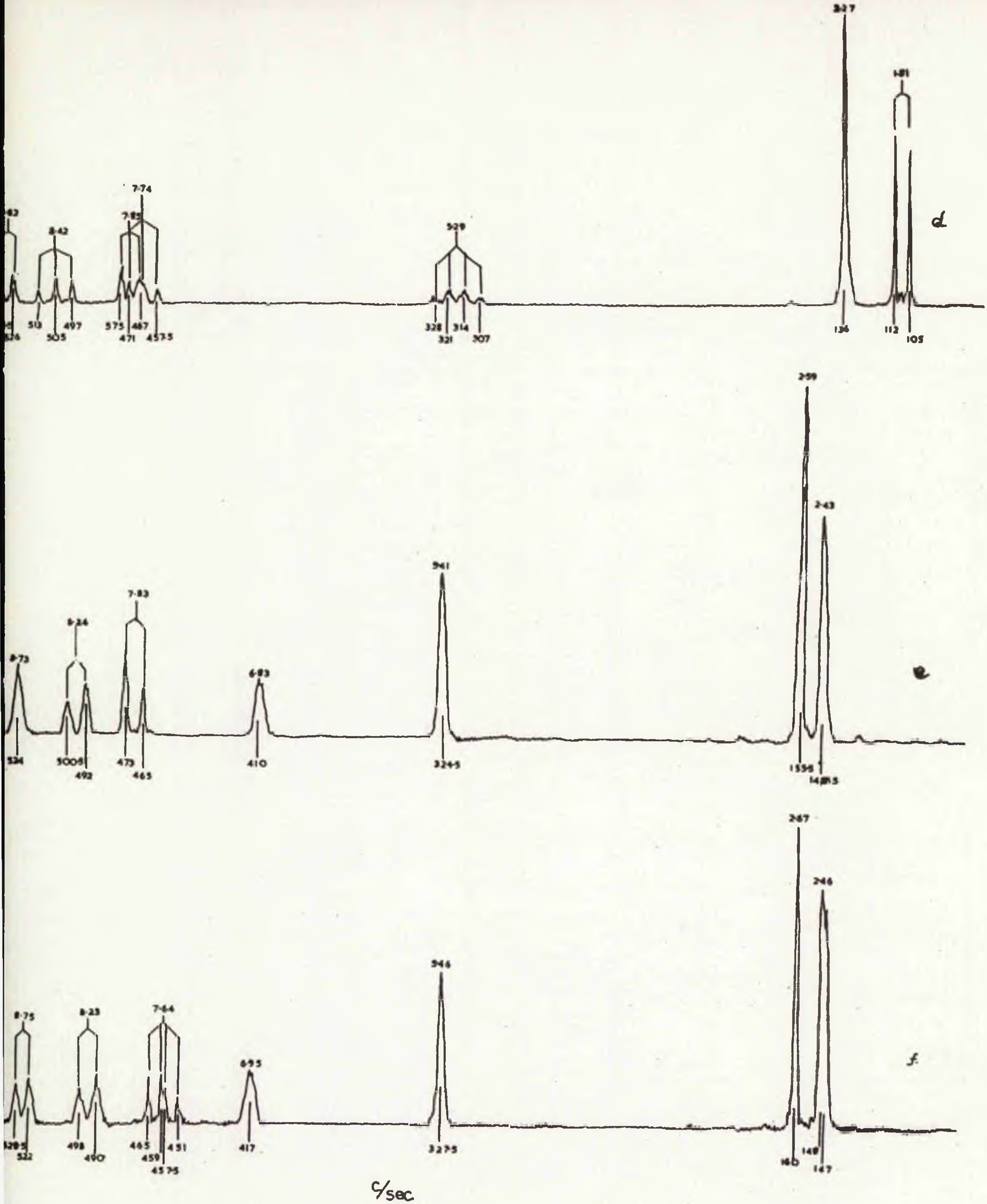
Perchlorate	Substituents.				
	1Me	2Me	3Me	$3-CH_2--CH_3$	2Ph
$l)_A$	2.45d J(Me-1 or -2 H-3) 1.5		1.74d J(Me-3 H-5)=7		7.52
$m)_A$		1.79			7.57

Unless otherwise indicated, values refer to singlet absorptions. For multiplets, d= doublet, t=triplet, m=multiplet q= quadruplet

* J= 0.5-1c/sec.

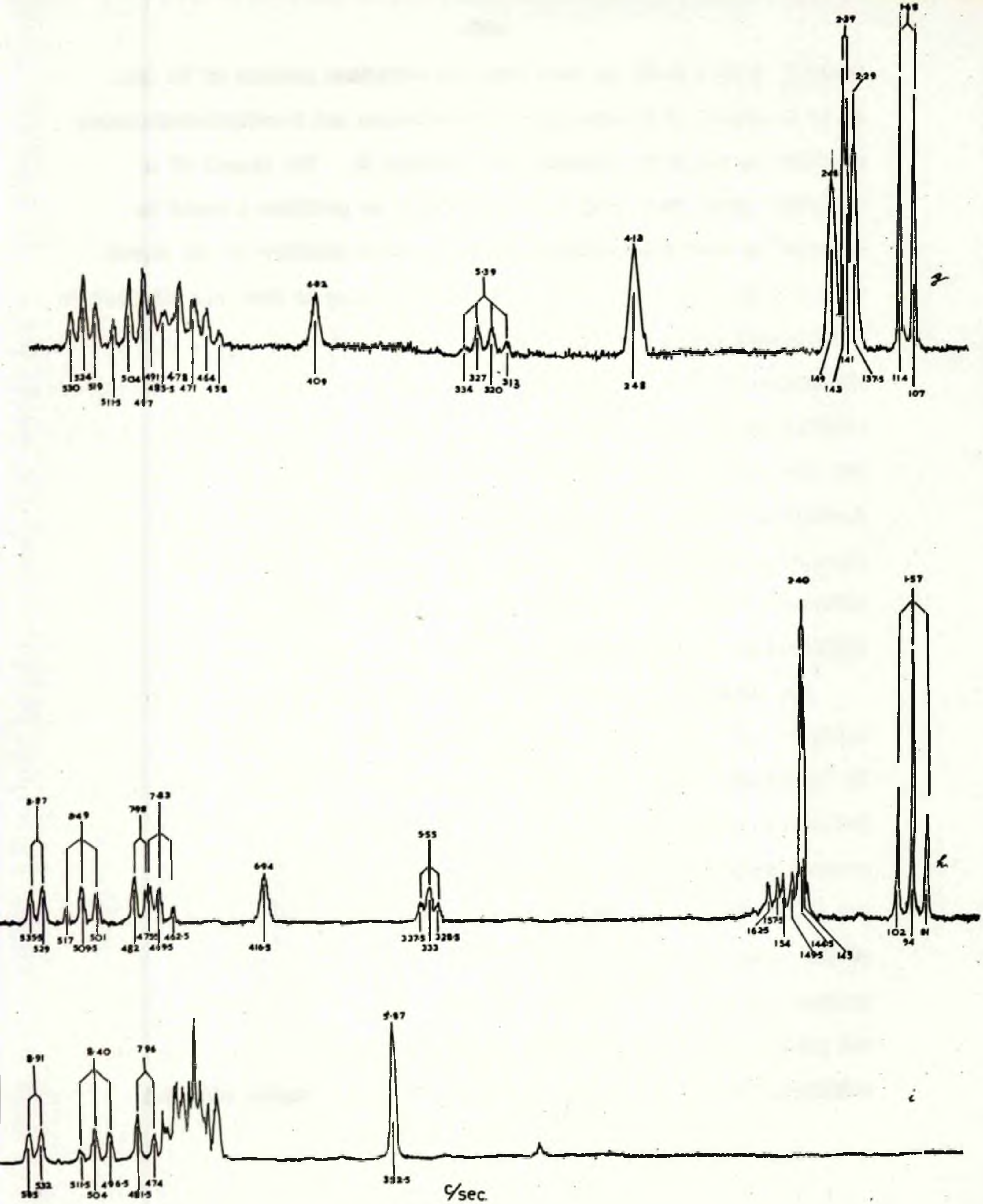
The spectrum of 7A(a) shows the following three features: (i) A single peak occurs at δ 5.55 which may be assigned to the protons of a methylene group on the basis of its spectral position (ii) Two doublets with equally spaced components occur at δ7.51 and at 7.19 (J = 6c./sec.) and clearly arise from an AB system of two protons (iii) The remaining signals occur at low-field in three groups comprising a doublet centred at δ 8.98 (J = 6.5 c./sec.), a triplet at δ 8.47 (J 7c./sec.), a complex signal consisting of a triplet at δ7.84 (J 7c./sec.) and a doublet at δ8.04 (J = 7.5 c./sec.). Integration of the spectrum shows that the single peak is equivalent to two protons, the AB quadruplet to two protons, and the low-field signals together to four protons.

Two features of the spectrum (a) of indolizinium perchlorate 7A (a) are also found in the spectra (b) and (c) of 2-methyl 7A (b) and


d
e
f
c/sec

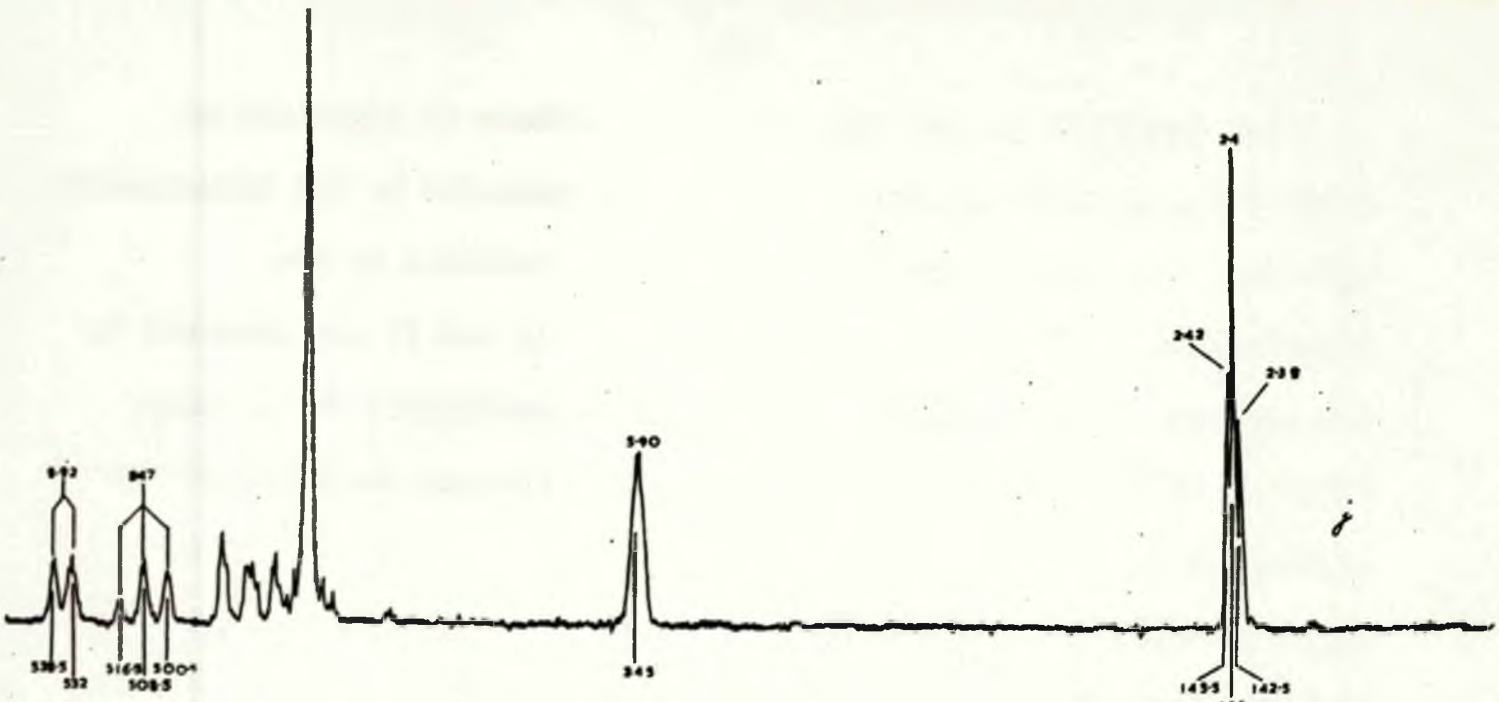
1,2-dimethyl-indolizinium perchlorate 7A (c). (i) The spectra of 7A (b) and 7A (c) show single peaks at δ 5.40 and at δ5.32 respectively, corresponding to the signal at δ 5.55 in 7A (a). (ii) They also show three groups of low-field signals, identical in pattern with those in the parent salt 7A (a). The integral curves of the spectra of 7A (b) and 7A (c) confirm the view that in each case the single peak corresponds to two protons and the low-field groups together to four protons as in the spectrum of the parent salt 7A (a). The spectrum (d) of 1,2,3,-trimethylindolizinium perchlorate 7A (d) shows one feature in common with (a), (b) and (c), namely, the three groups of low-field signals, whose integral curve also corresponds to four protons. The three low-field groups of signals of the four salts 7A (a-d) all occur in the same spectral region and, in each spectrum, are distinctly separated from all other peaks.

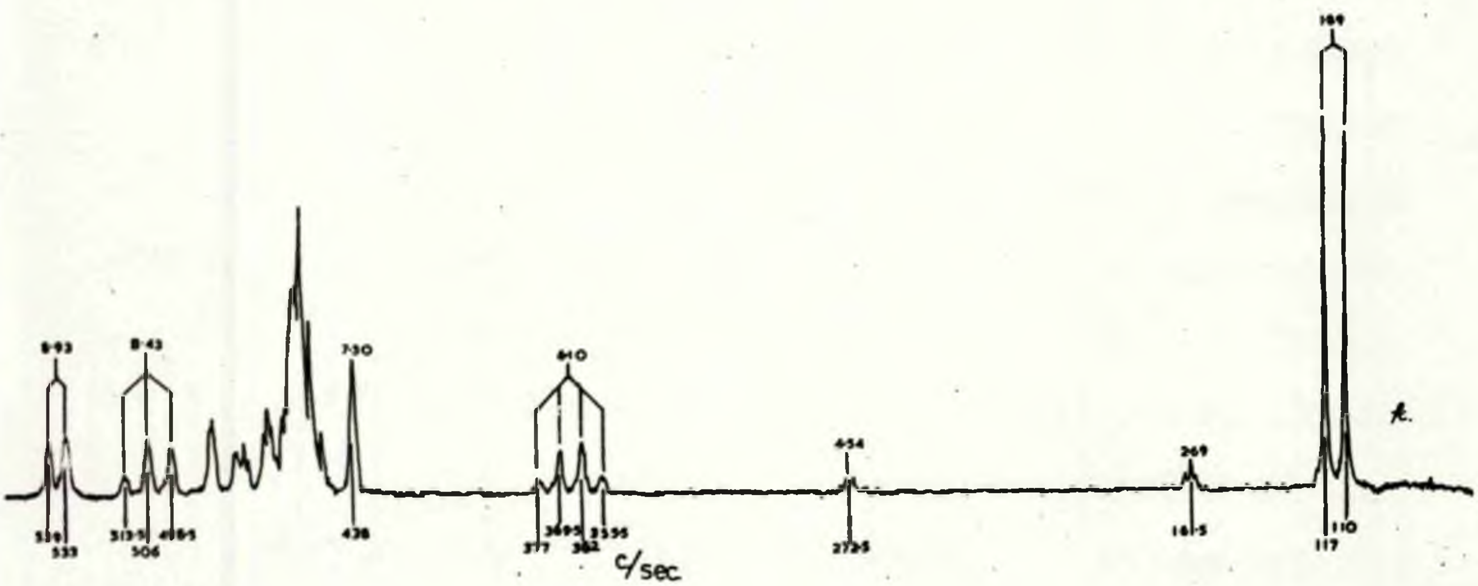
The pattern of the low-field group of signals is thus not altered by the progressive introduction of methyl groups into the positions 2,1 and 3. A small diamagnetic displacement only is observed. Therefore in all four salts, the four protons responsible for the low-field signals must be those at positions 5,6,7 and 8. These salts must consequently have resulted from protonation of the corresponding indolizines in the five membered ring. In the case of 1,2,-dimethylindolizinium perchlorate 7A (c) a methylene group can develop only by C-3 protonation. Since the signals from the methylene protons of 7A (a) and 7A (b) occur in the same narrow spectral

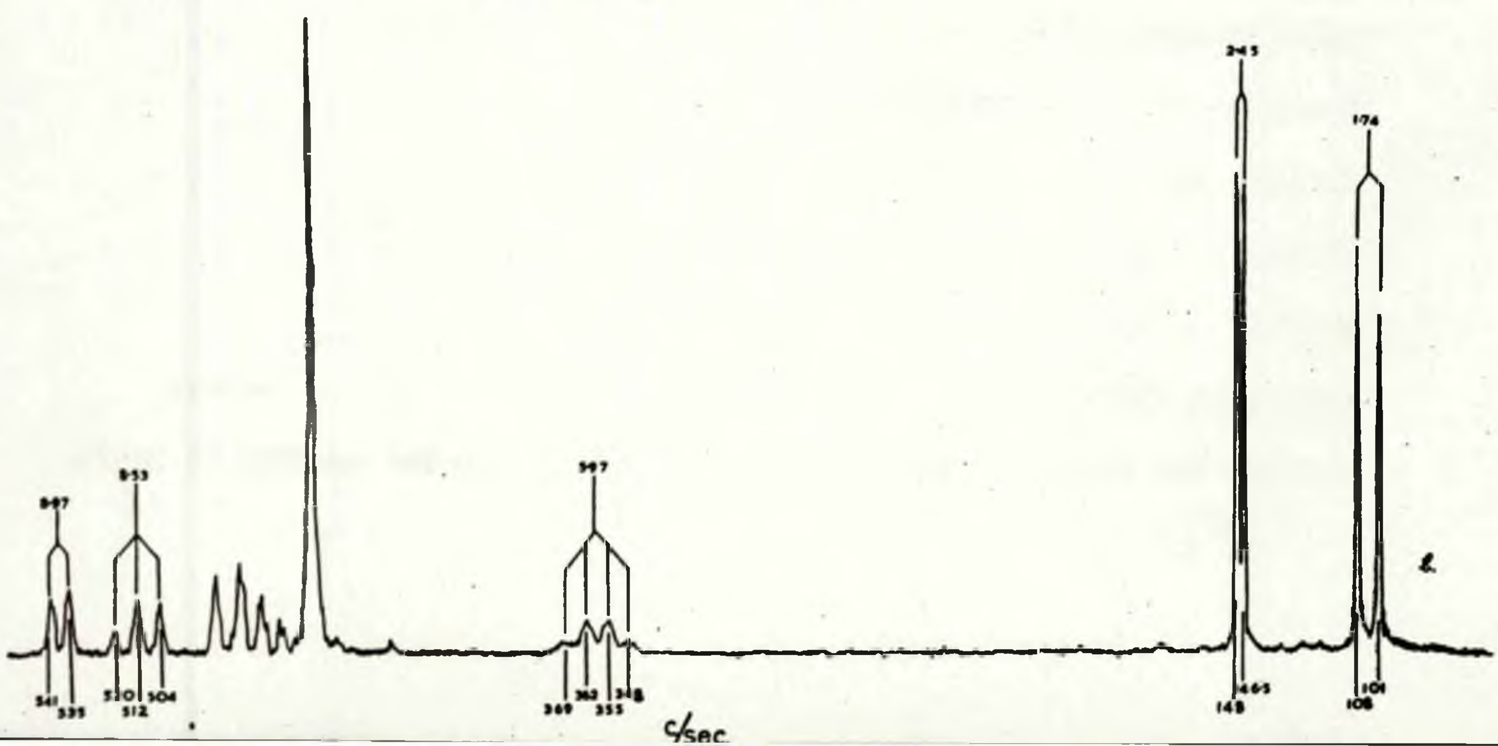

1.48
2.37
2.29
2.45
4.13
5.39
6.82
530 526 519 511.5 504 497 491 485.5 478 471 464 458
409
334 327 320 313
248
149 143 141 137.5 114 107
g
2.40
1.57
8.87
8.49
7.98
7.83
6.94
5.55
535.5 529 517 509.5 501 482 475.5 469.5 462.5
416.5
337.5 333 328.5
162.5 157.5 154 149.5 144.5 143
102 94 81
h
8.91
8.40
7.96
5.87
535 532 511.5 504 496.5 481.5 474
352.5
i
c/sec.

range (δ 5.56 - 5.32) as that from the methylene protons of 7A (c), it is concluded that indolizinium perchlorate and 2-methylindolizinium perchlorate are also protonated at position 3. The signal of a methylene group resulting from protonation at position 1 would be expected to show a substantial up-field shift relative to the signal from a 3-methylene group, since the latter group is directly attached to a positively charged nitrogen atom. The 1-methylene signal of the 1H-isomers of 2,3,-dimethyl-,7B (g), and 3-methyl-2-phenyl-indolizinium perchlorate 7B (k), occur at δ 4.13 and at δ 4.54 respectively. Thus the chemical shifts of the methylene protons of salts 7A (a-d) are consistent with direct linking of the methylene group to a positively charged nitrogen atom. The progressive up-field shift of the methylene signal in this series is the expected result of the introduction of electron releasing methyl groups.

The interpretation of the remaining features of the spectra of the salts 7A (a-d) are as follows (i) The AB quadruplet in the spectrum of 7A (a) arises from the spin-spin coupled pair H-1 and H-2. Although individual assignments cannot be made with certainty on the basis of present results, the high field components are tentatively assigned to H-1 rather than H-2 on the basis of a comparison with the H-1 signals of the salts 7A (b,e,f,g,h,i) (ii) The single peak at δ 6.83 in the spectrum of 2-methylindolizinium perchlorate arises from the isolated C-1 proton and the weakly split doublet ($J \sim 1$ c./sec.) at δ 2.41 is attributed to the 2-methyl group which is weakly coupled with H-1 through four bonds (iii) The two peaks at δ 2.25 and at δ 2.52 in the spectrum of 1,2-dimethylindolizinium perchlorate can probably be assigned to the 1- and 2- methyl groups respectively, since the 2-methyl group is nearer the deshielding influence of the positively charged nitrogen atom. The weak splitting in these signals could arise from spin-spin coupling over four or more bonds with the adjacent methyl or methylene group protons (iv) In the spectrum of 1,2,3-trimethylindolizinium perchlorate 7A (d) an evenly spaced quadruplet occurs at δ 5.29 (J = 7c/sec.) in place of the methylene singlets in spectra 7A (a-c) and is shown from the integral curves to correspond to one proton. The multiplicity arises from the spin-spin coupling of this proton with those of a methyl group linked to the same carbon atom. This is confirmed by the presence of a doublet centered at δ 1.81, showing the same splitting (J = 7c/sec.) and equivalent to three protons. The multiplicity of the single proton signal is independant evidence that protonation of 1,2,3-trimethylindolizinium perchlorate occur in the five membered ring and simultaneously strengthens the conclusion that protonation occurs in the five membered ring in the four salts 7A (a-d). From the occurrence of the quartet in the same spectral region as the methylene signalsin 7A (a-c) it is concluded that 1,2,3-trimethylindolizinium perchlorate also is protonated at the 3- position. The 1 and 2-methyl protons of 1,2,3-trimethylindolizinium perchlorate have identical chemical shifts, giving together a sharp signal at δ 2.27.


5·90
j


7·30
c/sec
k.


c/sec
l.

The low-field group of signals, whose pattern is identical in salts 7A(a,b,c,d,h) and whose pattern is complicated by the introduction of a 2-phenyl group in salts 7A(i,j,k,l), or modified by the introduction of 6- or 8- methyl groups in 7A (e and f) are examined in the representative spectrum of indolizinium perchlorate 7A (a) only. Recent work[121] has shown that the order of increased shielding of the pyridinium ion is H-2 < H-4 < H-3. By analogy, we assign the low-field doublet centred at δ8.98 in the spectrum of 7A (a) to H-5, the low-field triplet centred at δ8.47 to H-7, and the complex signal (quadruplet) to H-6 + H-8. The ratio (1:1:2) of the integrated intensities of these signals supports these assignments. The near equivalence of H-6 and H-8 results in H-7 signals being a triplet (disregarding the fine splitting due to meta coupling). The triplet centred at δ7.88 and the doublet at δ8.04, constituting the complex signal, are assigned to H-6 and H-8 respectively. These multiplets have one component (478.5 c./sec.) co-incident.

The spectra of 2,6-dimethylindolizinium perchlorate 7A (e), 2,8-dimethylindolizinium perchlorate 7A (f), 2-phenylindolizinium perchlorate 7A (i) and 1-methyl-2-phenylindolizinium perchlorate 7A (j) have the following spectral features in common with the salts 7A (a-c). (i) The occurrence of a singlet corresponding totwo protons in the same spectral region as that associated with a methylene signal in 7A (a-c). This signal in (e) and (f) occurs between the positions of the methylene signals in the spectra of salts

7A (a-c), and at lower field in the spectra (i) and (j) of salts 7A (i and j) due to the deshielding effect of the 2-phenyl substituent. Thus we conclude that the salts 7A (e,f,i,j) are also protonated at position 3. (ii) The signals due to H-1 in salts 7A (e,f,i,j) and the signals due to the 2-methyl group in salts 7A (e and f) and the 1-methyl group in 7A (j) likewise occur at the expected position (see Table I and spectra (e),(f), (i) and (j)). The weak splitting of the 1-methyl signal of salt 7A (j) into a triplet, is interpreted as arising from distant spin-spin coupling with the C-3 methylene protons.

The 6- and 8- methyl group signals in 7A (e and f) are shifted down-field relative to the 2-methyl signal in either of these salts or of 2-methylindolizinium perchlorate, owing to deshielding arising from the positively charged pyridinium structure. The presence of the 6- and 8- methyl groups modify the low-field group of signals. The resulting low-field group of signals are designated by virtue of their spectral position and multiplicity as follows: (i) The singlet at δ 8.73 in (e) is assigned to the isolated proton in the 5- position. (ii) The doublet centred at δ 7.83 (J = 8.5 c./sec.) is deduced to arise from H-8 spin-spin coupled to H-7, and the corresponding doublet at δ 8.26 (J = 8.5 c./sec.) to arise from H-7 spin-spin coupled to H-8.

(iii) The lower field doublet in (f) at 8.75 (J = 6.5 c./sec.) is attributed to H-5 spin-spin coupled with H-6; the doublet centred at δ 8.23 (J = 8 c./sec.) attributed to H-7 spin-spin coupled with H-6. (iv) The quadruplet in (f) centred at δ 7.64 (J = 6.5 and 8 c./sec.) is then attributed to a combination of H-6 spin-spin coupled with H-7 and H-5.

In the spectrum of salt 7A (i and j) the higher portion of the low-field group of signals is masked by the presence of a strong 2-phenyl absorption signal whose main peak in both salts occur at δ 7.52. The low-field doublet and triplet signals of H-5 and H-7 in the salts 7A (i,j,k,l) which contain a 2-phenyl group, are however still identifiable.

The spectrum of 1,3-dimethyl-2-phenylindolizinium perchlorate 7A (l), as may be anticipated, follows the pattern of that of 1,2,3-trimethylindolizinium perchlorate 7A (d), allowing for the replacement of a 2-methyl group by a 2-phenyl group. Thus the doublet of the 3-methyl group, the quadruplet of the 3-methine group, and a weakly split signal of the 1-methyl group all occur at the expected positions (Table I 7A(d) and 7A (l)). The splitting of the 1-methyl group signal into a doublet is interpretated to arise through the distant spin-spin coupling with H-3. Thus we conclude that protonation at C-3 also occurs in 1,3-dimethyl-2-phenylindolizinium perchlorate.

The positions of protonation in the salts 7 (g), 7 (h) and 7 (k) in which the 1-position is unsubstituted and the 2-and 3-positions are substituted poses an interesting question. Namely, will protonation, on steric grounds, preferentially occur at the vacant 1-position, or will C-3 protonation persist?

The spectrum of 2,3-dimethylindolizinium perchlorate 7 (g) is the most complex of the series and is comprised of the following signals: (i) Single peaks at δ 6.82, 4.13, 2.46 and at 2.29, (ii) a doublet at δ 1.68 (J = 7 c./sec.) and a weakly split doublet centred at δ 2.37 (J 2 c./sec.), (iii) an evenly spaced quadruplet centred at δ 5.59 (J = 7 c./sec.) and finally (iv) a complex low-field group of signals. It is apparent that all these signals cannot arise from one structural form of 2,3-dimethylindolizinium perchlorate (c.f. spectrum (c) of 1,2-dimethylindolizinium perchlorate). The spectral positions, integrated intensities and the identical splitting of the quadruplet at δ 5.59 (J = 7 c./sec.) and the doublet at δ 1.68 (J = 7 c./sec.) characterise these signals as resulting from the spin-spin interaction of a 3-methine and 3-methyl group. (c.f. salts 7A (d) and 7A (1) in Table I). Further, the spectral position of the single peak at δ 6.82 is in the region expected for an H-1 signal. These conclusions give adequate evidence for the presence of that form of the salt protonated at C-3 i.e. the presence of structure 7A (g).

The single peak at δ 4.13 is attributed to the protons of a C-1 methylene group, which as anticipated earlier, would be expected to occur at higher field than the signal from a C-3 methylene group.

Thus it would appear that protonation in 2,3-dimethylindolizinium perchlorate occurs at both the 3- and 1- positions. The proportions of the 3$\underline{H}$ and the 1$\underline{H}$- isomers are calculated from the integral curves to be 46% and 54% respectively.

The remaining high field signals in the region δ 2.48 - 2.29 are concluded to be methyl group signals which cannot be definitely assigned to any particular methyl group. It is tentatively suggested that the 2-methyl group in the 3$\underline{H}$- isomer is responsible for the weakly split doublet at δ 2.37 ($J \sim 2$ c./sec.). The multiplicity is then assumed to be due to spin-spin coupling with the C-3 methine proton. The isolated methyl groups at the 2- and 3- positions in the C-1 protonated isomer are then responsible for the two singlets at δ 2.29 and 2.46. The complex low-field signal arises from the combined effect of the 1$\underline{H}$- and 3$\underline{H}$- isomers.

The spectrum of 3-ethyl-2-methylindolizinium perchlorate 7A (h) consists of (i) a characteristic low-field pattern identical to that found in salts 7A (a-d). (ii) A singlet at δ 6.94, (iii) a triplet at δ 5.55, (iv) a complex signal, in which a weakly split doublet is prominent, in the region of 149.5 c./sec. and finally the occurrence of a triplet at δ 1.37. On the basis of the spectral position, contribution to the integrated intensity and multiplicity, the evenly spaced triplet at δ 5.55 (J = 4.8 c./sec.) is attributed to the signal from a C-3 methine proton (c.f. salt 7A (d) in Table I) which is coupled to two equivalent protons, namely, the methylene protons of the ethyl substituent. From similar considerations this methylene group is deduced to be responsible for the splitting of the signal of the adjacent methyl group into a triplet at δ 1.53 (J = 8 c./sec.) The signal of the isolated C-1 proton at δ 6.94 and the 2-methyl group at δ 2.40 occur at the expected positions (see Table I). The weak splitting of the 2-methyl signal into a doublet is interpreted to arise from spin-spin coupling through four bonds with either the C-1 or C-3 protons. The remainder of the complex high-field signal must then arise from the theoretically predicted eight-fold splitting of the signal from the methylene protons by the adjacent methine proton and methyl group. (This methyl group together with the methylene group constitutes the ethyl substituent). All the signals in 3-ethyl-2-methylindoliziniun perchlorate can be accounted for and agree with exclusive protonation at the 3-position.

The prominent peaks of the spectrum of 3-methyl -2-phenylindolizinium perchlorate 7 (k) are as follows: (i) a single peak at δ 7.30, (ii) a doublet centered at δ 1.89 (J = 7 c./sec.), (iii) a quadruplet at δ 6.10 (J ~ 7.5 c./sec.) and (iv) the low-field group of signals in which the strong phenyl absorption, the H-5 doublet and H-7 triplet are readily recognizable. From the occurrence of a quadruplet and doublet of identical splitting (J ~ 7-7.5 c./sec.) in the same spectral region in which these two signals occur in salt 7 A (d), and allowing for the small downfield displacement caused by the electron-withdrawing 2-phenyl group in place of a 2-methyl group, it can be concluded that these signals in salt 7 (k) also result from protonation at position 3.

On close examination the spectrum of 3-methyl-2-phenylindolizinium perchlorate (k) shows a small indistinct irregularity in the base line at δ 4.34 and a weakly split weak absorption triplet at δ 2.69. These two signals are postulated to arise from a small percentage of the 1H- isomer. The respective percentage of the 3H-and 1H- isomers of 3-methyl-2-phenylindolizinium perchlorate are calculated from the integral curve to be of the order of 90% and 10%. The weakly split triplet at δ 2.69 is attributed to the 3-methyl group, the multiplicity is suggested to arise from distant spin-spin coupling with the C-1 methylene protons. The indistinct irregularity may be a weakly split quadruplet attributed to the signal of a C-1 methylene group, the multiplicity of which is due to distant spin-spin coupling with the C-3 methyl protons.

The two spectra (b) and (i) which were obtained for 2-methyl- and 2-phenyl- indolizinium perchlorate using trifluoracetic acid as solvent were identically reproduced using deuterotrifluoracetic acid as solvent, thus showing that the 3-methylene protons of these salts do not exchange at a detectable rate with the solvent protons. It may be concluded that the cations from 1,2-, 2,6- dimethyl- and 1,2,3-trimethyl-indolizine, which are more basic than 2-methylindolizine (see tabulated basicities pages 11-12), also do not exchange in trifluoracetic acid. The cations from 2,8-dimethyl-, 1-methyl-2-phenyl-, 1,3-dimethyl-2-phenyl-indolizine, whose basicities, though not determined, would be expected to be comparable with if not greater than that of 2-methylindolizine. They would certainly be expected to exceed the unknown basicity of 2-phenylindolizine, and thus would not be expected to exchange in trifluoroacetic acid. The possibility that the cations derived from the less basic 2,3,-dimethyl-, 3-ethyl-2-methyl-, and 3-methyl-2-phenyl-indolizine do not undergo proton exchange with the solvent, though unlikely can not be excluded with certainty.

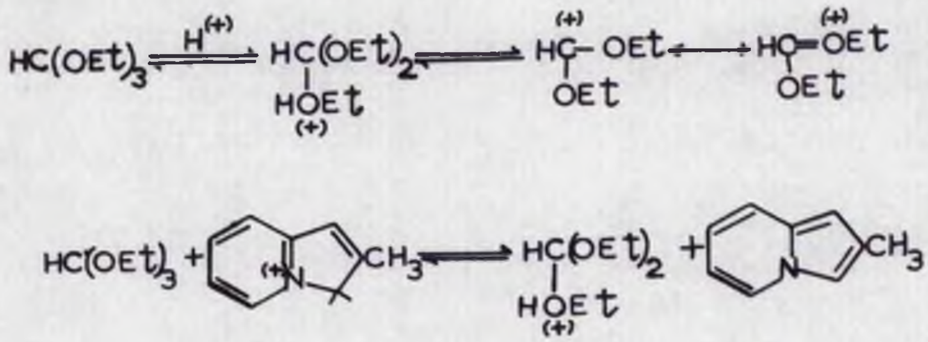
BII$_4$ Conclusions from Proton Magnetic Resonance Studies on Indolizinium Perchlorates (a - l).

The salts 7A (a,b,c,e,f,i,j) in which the 3-position is unsubstituted, are protonated at the 3-position. The signal from the resulting methylene group is in the region δ5.32 - 5.90. The spread of 0.7 in δ values is attributed to the variable shielding effects of methyl substituents in salts 7A (a,b,c,e,f) and the deshielding effect of a 2-phenyl substituent in salts 7A (i and j).

The salts 7A (d and l) in which all three positions of the five-membered ring are substituted are also protonated at position 3. The C-3 methine signal is split by spin-spin coupling with the C-3 methyl group into an evenly spaced quadruplet which is found in the same spectral region (δ5.29 and 5.97 respectively) as the signal attributed to C-3 methylene in the salts 7A (a,b,c,e,f,i,j).

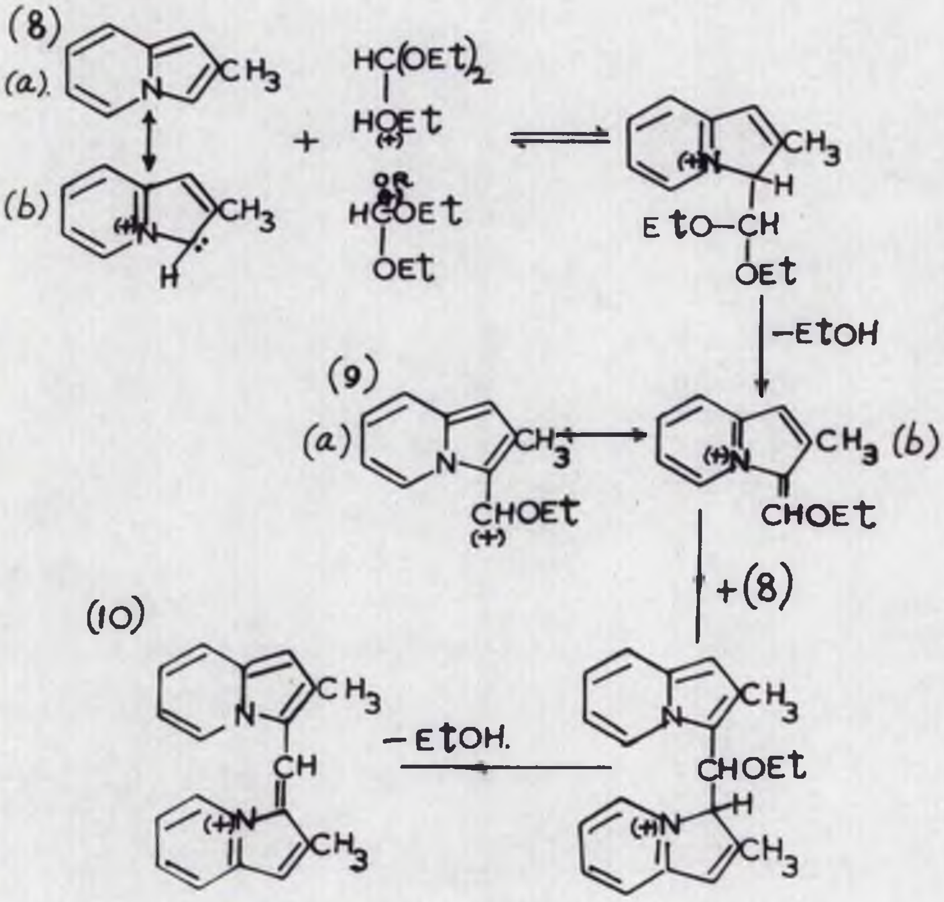
We deduce from the spectra of the salts 7 (g,h,k), in which both the 2- and 3- positions are substituted and the 1-position is unsubstituted, that (i) protonation of 3-ethyl-2-methylindolizine occurs exclusively at position 3, (ii) protonation of 3-methyl-2-phenylindolizine occurs predominantly at position 3. (iii) Protonation of 2,3-dimethylindolizine occurs to an almost equal extent at the 3- and 1- positions. It would appear therefore, that the steric effect is of sufficient importance in 2,3-dimethyl and 3-methyl-2-phenylindolizinium perchlorates as to direct protonation at least in part, to the sterically unhindered 1-position. The replacement of a 2-methyl group in 2,3-dimethylindolizinium perchlorate 7 (g) by a 2-phenyl group to give salt 7 (k) apparently deactivates the 1- rather than the 3-position and thus partly restores this position as that favoured for protonation. The exclusive protonation at the 3-position in 3-ethyl-2-methylindolizinium perchlorate 7A (h) must arise from a sufficiently great increase in the electron density produced by an increased inductive effect at position 3 to offset the slight increase in the steric effect caused by the replacement of a methyl by an ethyl group.

FIG. 1



HC(OEt)3
H(+)
HC(OEt)2
HOEt
(+)
HC- OEt
OEt
HC=OEt
OEt
HC(OEt)3 +
CH3
N

FIG. 2



(8)
(a).
(b)
CH3
N
H
HC(OEt)2
HOEt
OR
HCOEt
OEt
EtO-CH
-EtOH
(9)
(a)
(b)
CHOEt
+(8)
(10)
CH
-EtOH.

BIII Ethoxymethyleneindolizinium Salts.

In view of the results[122] obtained in a study of the action of ethyl orthoformate on azulenes in the presence of acids, a parallel investigation has been carried out on indolizines. The acid catalysed condensation was most readily effected by the action of a large excess of ethyl orthoformate on an alcoholic solution of the indolizinium perchlorate. Reaction is considered to take place according to the scheme outlined in Fig. 2, illustrated for the condensation with 2-methylindolizine.

There aretwo factors which determine the possible isolation of the ethoxymethyleneindolizinium perchlorate represented by the resonance hybrid ((9) a-b). Firstly there is the stability of the ethoxymethyleneindolizinium salt. This is influenced by the number and position of electron-attracting or - donating substituents in the indolizine nucleus. Electron-donating substituents reduce the electrophilic nature of the exocyclic methine carbon atom and so stabilises the structure ((9) a) which accommodates the positive charge in the pyridinium moiety, rather than ((9) b) in which the positive charge resides on the exocyclic carbon atom. Secondly, the nucleophilic reactivity of the indolizine is important. This affects the successful attack of the ethoxymethyleneindolizinium cation on unreacted indolizine, which is presumably released from the indolizinium salt by the action of the excess ethyl orthoformate via the equilibrium shown in Fig. 1., and results in the formation of symmetrical monomethine dye (10). The nucleophilic reactivity would also be enhanced by the presence of electron-donating substituents which would facilitate the development of the dipolar reacting structure ((8)b).

It would appear from the experimental results that the firstly mentioned factor predominates and only indolizines in which inductive or inductive and mesomeric effects operate can be readily isolated as stable ethoxymethyleneindolizinium salts. Ethoxymethylene-indolizinium salts were obtained from all the indolizinium perchlorates prepared except 1,2,3-trimethyl- and 1,3-dimethyl-2-phenyl-indolizinium perchlorates. Here no reaction occurred, thus establishing that reaction occurs at the 1- or 3- positions, and substantiating to some extent the mechanism of the reaction shown in Fig.2. Ethoxymethyleneindolizinium perchlorates were shown to exist transiently in the case of indolizine, 2-phenylindolizine and benzo (*e*) indolizine (i) by the formation of dimethinecyanine dyes with 2,3-dimethylbenzothiazolium perchlorate and (ii) by the formation of the corresponding aldehydes from indolizine and 2-phenylindolizine (see CIV 24-26 and $CVIb_1$, $CVIb_2$). Ethoxymethyleneindolizinium salts in which the electrophilic nature of the cation is sufficiently suppressed by the presence of at least one alkyl group were isolated in good to nearly quantitative yields, as yellow or green crystalline salts from blue solutions containing varying concentrations of the symmetrical monomethine dye salts. The concentration of this dye salt increases with increase in electrophilic reactivity of the 3 (1)-ethoxymethyleneindolizinium cation which increases approximately according to the following order: 3-ethoxymethylene-1,2-dimethylindolizinium, 3-ethoxymethylene-1-methyl-2-phenylindolizinium, 1-ethoxymethylene-3-ethyl-2-methylindolizinium, 1-ethoxymethylene-2,3-dimethylindolizinium, 1-ethoxymethylene-2-phenyl-3-methylindolizinium, 1-ethoxymethylene-3-methyl-2-phenylindolizinium, 3-ethoxymethylene-2,8-dimethylindolizinium, 3-ethoxymethylene-2,6-dimethylindolizinium, 3-ethoxymethylene-2-methyl-1-phenylindolizinium, 3-ethoxymethylene-2-methylindolizinium, 3-ethoxymethylene-2-phenylindolizinium, 3-ethoxymethyleneindolizinium, 3-ethoxy methylene benzo (g) indolizinium. The concentration of a monomethine dye salt resulting from the condensation of ethyl *ortho*formate with a given indolizinium perchlorate increases with decrease in the molar proportion of ethyl *ortho*formate and elevation in the reaction temperature.

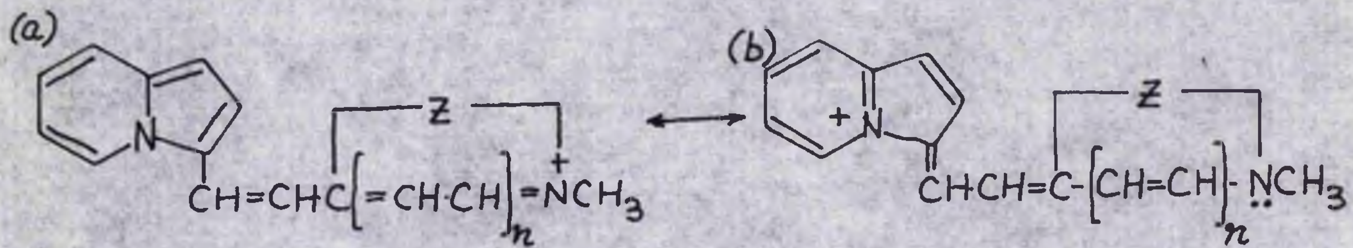
XIV Condensation Reactions of 3 (1)-Ethoxymethyleneindolizinium Salts.

3(1)-Ethoxymethyleneindolizinium salts were found to condense under suitable conditions with a number of several classes of compounds to form novel types of cyanine dyes.

XIV$_1$ Condensation of 3(1)-Ethoxymethyleneindolizinium Salts with Heterocyclic Quaternary Ammonium Salts.

3(1)-Ethoxymethyleneindolizinium salts condense in the presence of organic bases (piperidine, diethylamine) with various heterocyclic quaternary ammonium salts which contain a reactive methyl group, to form members of a class of dimethine cyanine dye salts (11). (n = 0 or 1; Z is the residue of a heterocyclic nucleus). The methyl group in the heterocycle is situated so that resonance occurs in the product between structure (11)a in which the positive charge is carried by the quaternary nitrogen, and structure (11)b in which the positive charge completes the pyridinium moiety of the indolizinium structure.

(11)



Heterocycles whose quaternary salts reacted with 3(1)-ethoxymethyleneindolizinium salts were 2- and 4- methyl-pyridines, and -

quinolines, 2-methyl-benzoxazole and -benzothiazole, 2-methyl and 2,4-dimethyl-thiazole. The visible absorption data of the twenty-six dimethinecyanine salts prepared are listed in table II, and the visible absorption spectrum of 3-methyl-2-(2-(2-methylindolizin-3-yl) vinyl) benzoxazolium perchlorate, a typical example of such dimethinecyanine dye salts, is shown on plate I.

TABLE XI

Visible absorption maxima of dimethinecyanine salts in methanol containing 2% $(\frac{V}{V})$ perchloric acid.

CATION	Anion	λ max.	Log ε
3-Methyl-2-(2-(indolizin-3-yl)vinyl)benzothiazolium	ClO_4	387	4.70
3-Methyl-2-(2-(2-methylindolizin-3-yl)vinyl) benzoxazolium	ClO_4	519	4.93
1-Methyl-4-(2-(2-methylindolizin-3-yl)vinyl) pyridinium	ClO_4	521	4.75
3-Methyl-2-(2-(2-methylindolizin-3-yl)vinyl) thiazolium	ClO_4	525	4.68
3-Methyl-2-(2-(2-methylindolizin-3-yl)vinyl) benzothiazolium	ClO_4	530	4.91
1-Methyl-2-(2-(2-methylindolizin-3-yl)vinyl) quinolinium	ClO_4	563	4.89
1-Methyl-4-(2-(2-methylindolizin-3-yl)vinyl) quinolinium	ClO_4	595	4.73
1-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl) pyridinium	I	551	4.65
1-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl) pyridinium	ClO_4	531	4.66
3-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl) benzoxazolium	ClO_4	534	4.95
1-Methyl-4-(2-(1,2-dimethylindolizin-3-yl)vinyl) pyridinium	ClO_4	556	4.70
3-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl) thiazolium	ClO_4	542	4.70
3,4-Dimethyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl) thiazolium	ClO_4	544	4.80
3-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl) benzothiazolium	ClO_4	571	4.96
1-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl) quinolinium	ClO_4	573	4.86
1-Methyl-4-(2-(1,2-dimethylindolizin-3-yl)vinyl) quinolinium	I	621	4.76

TABLE II continued

CATION	Anion	$\lambda_{max.}$	Log ε
3-Methyl-2-(2-(2,6-dimethylindolizin-3-yl)vinyl) benzoxazolium	ClO_4	527	4.97
3-Methyl-2-(2-(2,6-dimethylindolizin-3-yl)vinyl) thiazolium	ClO_4	585	4.68
3-Methyl-2-(2-(2,6-dimethylindolizin-3-yl)vinyl) benzothiazolium	ClO_4	561	4.96
1-Methyl-4-(2-(2,6-dimethylindolizin-3-yl)vinyl) quinolinium	ClO_4	609	4.81
3-Methyl-2-(2-(2,8-dimethylindolizin-3-yl)vinyl) benzothiazolium	ClO_4	557	4.95
3-Methyl-2-(2-(2-phenylindolizin-3-yl)vinyl) benzothiazolium	ClO_4	585	4.78
3-Methyl-2-(2-(1-methyl-2-phenylindolizin-3-yl)vinyl) benzoxazolium	ClO_4	558	4.90
3-Methyl-2-(2-(1-methyl-2-phenylindolizin-3-yl)vinyl) benzothiazolium	ClO_4	573	4.93
3-Methyl-2-(2-(3-methyl-2-phenylindolizin-1-yl)vinyl) benzoxazolium	ClO_4	508	4.96
3-Methyl-2-(2-(benzo (*e*) indolizin-3-yl)vinyl) benzothiazolium	ClO_4	561	5.18

From Table II the following conclusions regarding the position of the absorption maxima can be drawn. (i) Alkylation of the indolizine nucleus produces in all cases a bathochromic displacement of λ max. (ii) Replacement of the 2-methyl group by a 2-phenyl group, of the indolizine component in the dimethinecyanine dye salt, resulting from the condensation of 3-ethoxymethylene-2-methylindolizinium perchlorate with 2,3-dimethylbenzoxazolium perchlorate causes a hypsochromic shift in λ max. A similar replacement of a 2-methyl by a 2-phenyl group in the dimethinecyanine dye salt resulting from the condensation of 3-ethoxymethylene-1,2-dimethylindolizinium perchlorate, however, produces a small bathochromic shift in λ max. (iii) The only dimethinecyanine salt formed by condensation with 1-ethoxymethylene-3-methyl-2-phenylindolizinium perchlorate with 2,3-benzoxazolium perchlorate shows a hypsochromic shift of 30 mμ when compared with the isomeric salt formed by condensation of 3-ethoxymethylene-1-methyl-2-phenylindolizinium perchlorate. This is presumably due to shortening of the cyanine chain when condensation occurs at C-1 rather than C-3. (iv) In each series, with the same indolizine nucleus, the absorption maxima shifts to longer wavelength as the heterocyclic component is changed in the order, 2-pyridine, 2-benzoxazole, 4-pyridine, 2-thiazole, 2-(4-methylthiazole), 2-benzothiazole, 2-quinoline, 4-quinoline. This order, in which the adsorption maxima shifts to longer wavelength as the heterocyclic component is changed, is closely followed (with the exception that 4-pyridine precedes

FIG.3

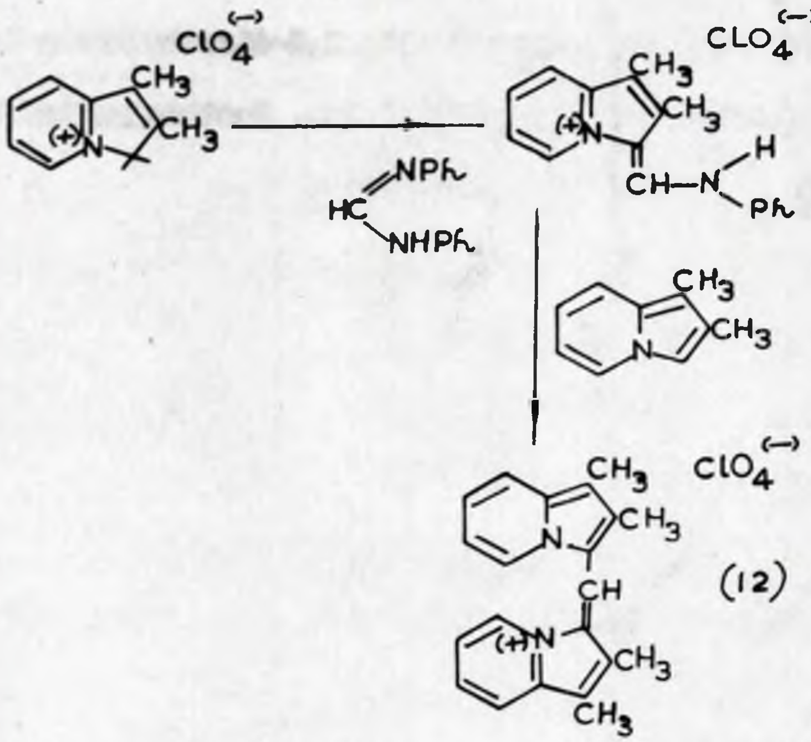
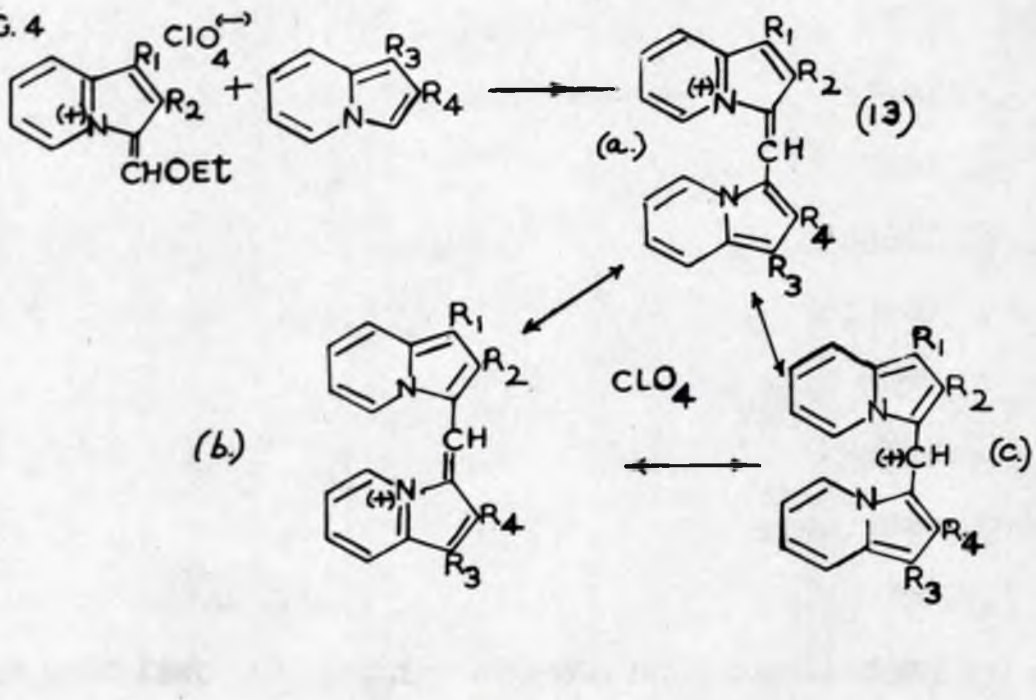


FIG. 4



2-benzoxazole) in dimethinecyanine dye salts resulting from a similar series of condensations between 1(3)-formylazulenes and heterocyclic quaternary ammonium salts.[123] (v) The following sequence in order of increasing λ max is observed for the 3(1)-ethoxymethylene-indolizinium perchlorates condensed with 2,3-dimethylbenzothiazolium perchlorate: 3-ethoxymethyleneindolizinium, 3-ethoxymethylene-2-phenylindolizinium, 3-ethoxymethylene-2-methylindolizinium, 3-ethoxymethylene-2,8-dimethylindolizinium, 3-ethoxymethylene-2,6-dimethylindolizinium and 3-ethoxymethylene benzo (e) indolizinium, 3-ethoxymethylene-1,2-dimethylindolizinium, 3-ethoxymethylene-1-methyl-2-phenyl-indolizinium.

BIV$_2$ Indolizinylmethyleneindolizinium Perchlorates.

The condensation of 1,2 and 2,3-dimethyl-indolizines with 1(3)-anilinomethylene-1,2 and 2,3-dimethylindolizinium perchlorates leads to the formation of (1,2 and 2,3-dimethylindolizin-3(1)-yl) methylene-1,2- and -2,3-dimethylindolizinium perchlorates, respectively.[124] The 1(3)-anilinomethylene-1,2 or 2,3-dimethyl-indolizinium perchlorate is prepared by the condensation of diphenyl-formamidine in acetic anhydride, with 1,2 or 2,3-dimethyl-indolizines. The reaction scheme is shown in Fig. 5 for the formation of (1,2-dimethylindolizin-3-yl) methylene 1,2-dimethylindolizinium perchlorate (12).

Indolizin-3(1)-yl methyleneindolizinium perchlorates have been prep(
as intensely blue-violet coloured salts by the following three

methods.

(i) The condensation of 3 (1)-ethoxymethyleneindolizinium perchlorates with an alcoholic solution of indolizines yields symmetrical (Fig. 4 ($R_1 = R_3$ and $R_2 = R_4$) or unsymmetrical (Fig. 4 $R_1 \neq R_3$ or $R_2 \neq R_4$) monomethine dye salts. The reaction may be regarded as an electrophilic attack of the ethoxymethyleneindolizinium perchlorate at the reactive, unsubstituted 1- or 3- positions of the indolizine. The resulting monomethine dye salt (13) is stabilised by resonance involving the structures ((13)a) in which the positive charge confers the indolizinium cationic structure on one of the indolizine nuclei, the other nucleus being uncharged, (b) in which the roles of the two indolizine nuclei are exchanged and (c) in which the positive charge resides on the exocyclic methine carbon atom.

(ii) The condensation of 3 (1)-formylindolizines with indolizinium perchlorates also gives unsymmetrical and symmetrical monomethine dye salts.

(iii) The condensation of ethyl orthoformate with two molecular proportions of indolizines yields symmetrical monomethine salts according to the mechanism outlined in Fig. 2 and discussed in section B III. The visible absorption data for the prepared monomethine dye salts are given in Table III.

TABLE XXI

Visible absorption maxima of indolizinylmethyleneindolizinium perchlorates in methanol containing 2% ($\frac{V}{V}$) perchloric acid.

CATION	Anion	λmax.	Log ε
3-(Indolizin-3-yl)methyleneindolizinium	ClO_4	573	
3-(2-Methylindolizin-3-yl) methylene-2-methyl-indolizinium	ClO_4	582	4.63
3-(2-Methylindolizin-3-yl) methylene-1,2-dimethylindolizinium	ClO_4	593	4.64
3-(2-Methylindolizin-3-yl) methylene-2,6-dimethylindolizinium	ClO_4	597	4.64
3-(2-Methylindolizin-3-yl) methylene-2,8-dimethylindolizinium	ClO_4	591	4.57
3-(2-Methylindolizin-3-yl) methylene-1-methyl-2-phenylindolizinium	ClO_4	620	4.52
3-(1,2-dimethylindolizin-3-yl) methylene-1,2-dimethylindolizinium	ClO_4	630	4.62
1-(2,3-dimethylindolizin-1-yl) methylene-2,3-dimethylindolizinium	ClO_4	586	
3-(1,2-dimethylindolizin-3-yl) methylene-1-methyl-2-phenylindolizinium	ClO_4	636	4.63
3-(2,8-dimethylindolizin-3-yl) methylene-1-methyl-2-phenylindolizinium	ClO_4	628	4.50
3-(2,6-dimethylindolizin-3-yl) methylene-1-methyl-2-phenylindolizinium	ClO_4	652	4.51
3-(benzo (c) indolizin-3-yl) methylene benzo (c) indolizinium	ClO_4	561	

The following conclusions may be drawn: Firstly, alkylation of either indolizine nucleus results in a bathochromic displacement of the absorption maximum. Secondly, for a series of monomethine dye salts in which one of the indolizine nuclei is 2-methylindolizinium the absorption maximum shifts progressively to longer wavelengths in the order, (2-methylindolizin-3-yl) methylene, (2,8-dimethylindolizin-3-yl) methylene, (1,2-dimethylindolizin-3-yl) methylene, (2,6-dimethylindolizin-3-yl) methylene. This order is repeated for the series in which one of the indolizine nuclei is 1-methyl-2-phenylindolizinium. Thirdly, condensation of the indolizine nuclei, constituting the monomethine dye salt at the1- rather than the 3-position produces a hypsochromic displacement, thus the absorption maxima of (1,2-dimethylindolizin-3-yl) methylene-1,2-dimethylindolizinium perchlorate occurs at 680 mμ whereas that of (2,3-dimethylindolizin-1-yl) methylene -2,3-dimethylindolizinium perchlorate occurs at 586 mμ. This displacement is again suggested to be due to shortening of the cyanine chain when condensation occurs at the 1-position. The visible absorption spectrum of (1,2-dimethylindolizin-3-yl) methylene-1,2-dimethylindolizinium perchlorate is shown on plate I .

FIG.5

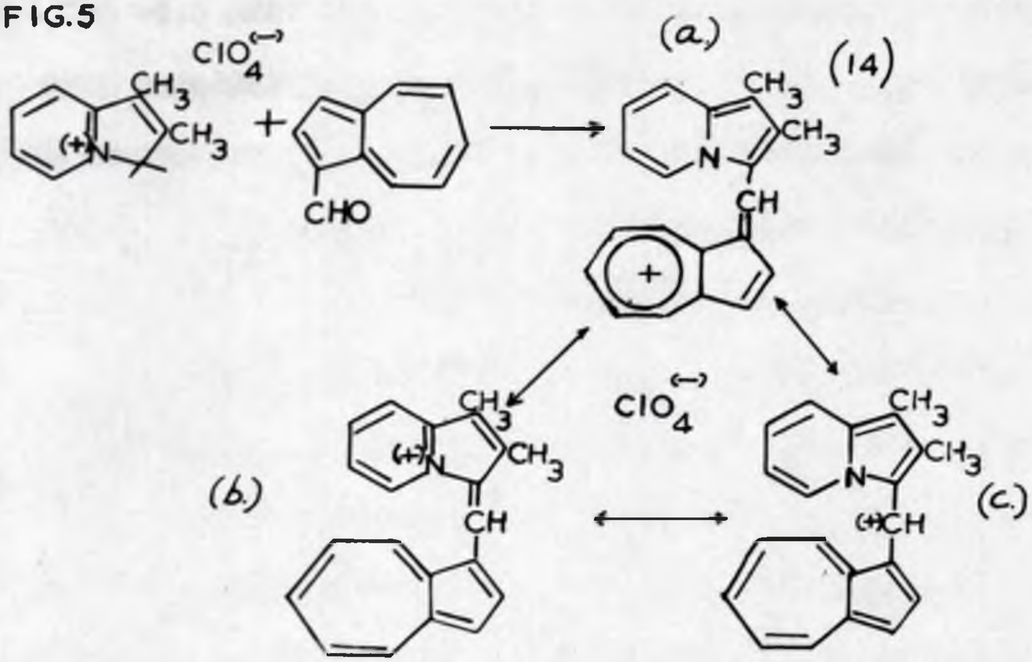
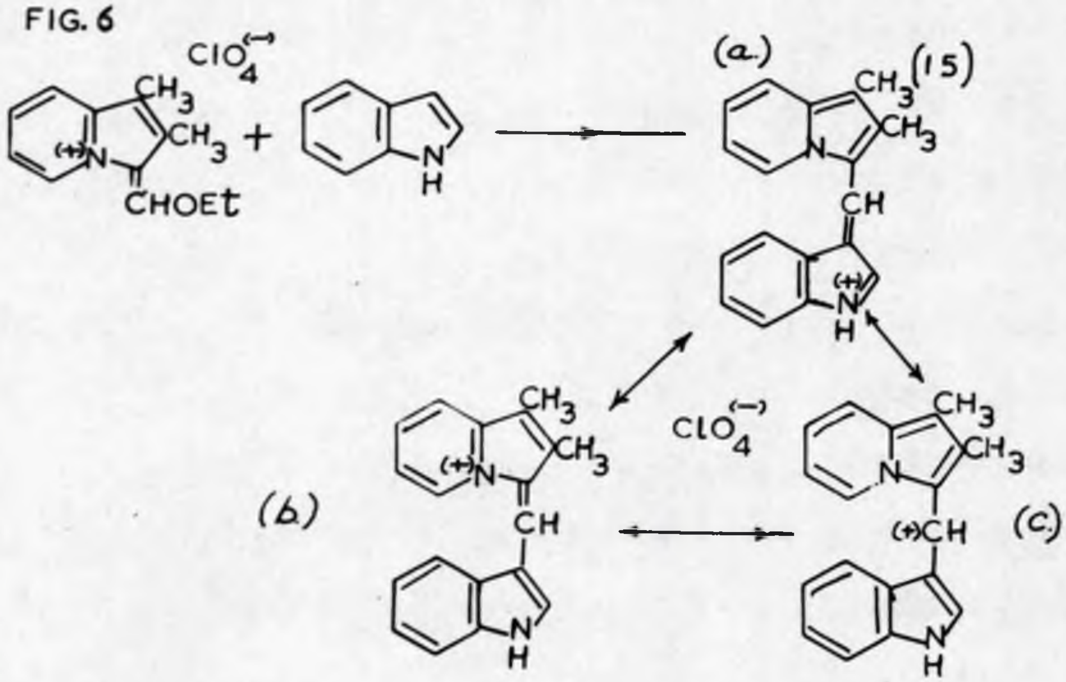


FIG. 6



BIV$_5$ 3-(Azulen-1-yl) and 3-(Indol-3-yl) Methyleneindoliziniun Salts.

Stepanov and Aldanova[125] reported the formation of mixed azulene-indolizine monomethine cyanine dye salts by the acid catalysed condensation of 1-formylazulene with 1,2- and 2,3-dimethylindolizines. A number of mixed azulene-indolizine monomethine cyanine dye salts were prepared in an analogous manner (CVc), exemplified by the preparation of 3-(azulen-1-yl) methylene-1,2-dimethylindolizinium perchlorate (Fig. 5 (14)) whose visible absorption spectrum is shown on plate I. The formation of such cyanine dye salts can be achieved equally well by the condensation of an azulene with an ethoxymethyleneindolizinium perchlorate (CVd).

Similarly, 3-(indol-3-yl) methyleneindolizinium iodides were prepared by the condensation of ethoxymethyleneindolizinium iodides with an ethanolic solution of indole, Fig. 6, (CVe). The structures of both the azulene-indolizine and indole-indolizine mixed monomethine cyanine dye salts are stabilised by resonance involving forms of the type ((14) a,b, and c) and ((15) a,b, and c) respectively; analogous to those for the indolizine-indolizine monomethine dye salts ((13) a, b and c). The positive charge in ((14)a) is delocalised within the seven membered ring of the azulene as a tropylium cation, whereas the positive charge in ((15)a) will be mainly associated with the nitrogen atom of the indole nucleus.

TABLE IV

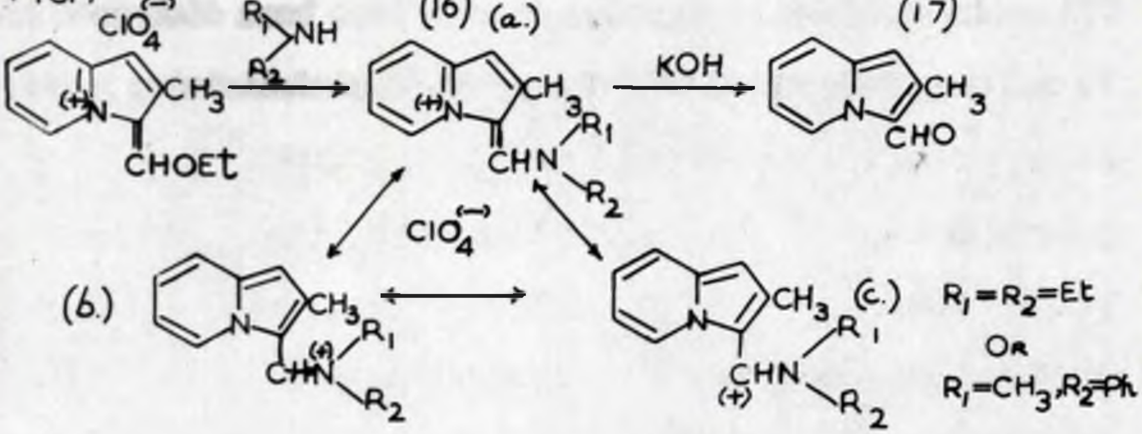
Visible absorption maxima of 3-(azulen-1-yl) methyleneindolizinium perchlorates in methanol containing 1% $\left(\frac{V}{V}\right)$ perchloric acid.

CATION	Anion	λmax.	Log ε
3-(Azulen-1-yl) methylene-2-methylindolizinium	ClO_4	575	4.65
3-(Azulen-1-yl) methylene-1,2-dimethylindolizinium	ClO_4	568	4.58
3-(Azulen-1-yl) methylene-2,6-dimethylindolizinium	ClO_4	566	4.64
3-(3-Methylazulen-1-yl) methylene-2-methylindolizinium	ClO_4	608	4.68
3-(3-Methylazulen-1-yl) methylene-1,2-dimethyl-indolizinium	ClO_4	604	4.68
3-(3-Methylazulen-1-yl) methylene-2,6-dimethyl-indolizinium	ClO_4	605	4.66
3-(3,8-dimethyl-5-isopropylazulen-1-yl) methylene-1,2-dimethylindolizinium	ClO_4	648	4.68

The visible absorption data for the azulene-indolizine mixed monomethine dye salts is shown in Table IV, from which the following conclusions can be drawn.

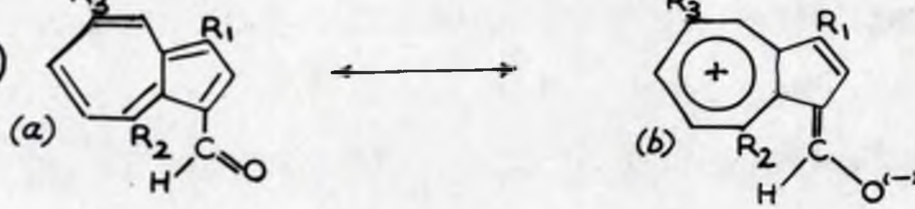
(i) Increase in alkylation of the azulene nucleus produces a bathochromic displacement of λ max. (ii) In contrast increase in alkylation of the indolizine nucleus produces a small hypsochromic displacement in λ max.

FIG. 7



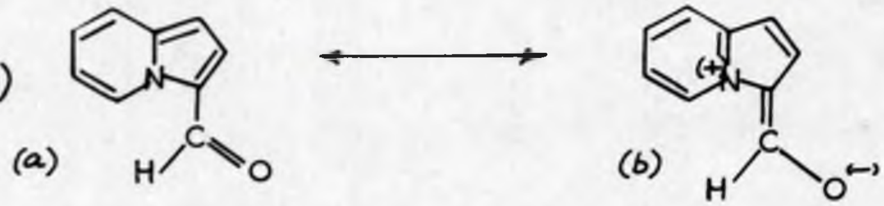
(16) (a.)
(17)
$ClO_4^{(-)}$
R_1R_2NH
KOH
CH_3
CHOEt
CHO
(b.)
(c.)
$R_1 = R_2 = Et$
Or
$R_1 = CH_3, R_2 = Ph$

(18)



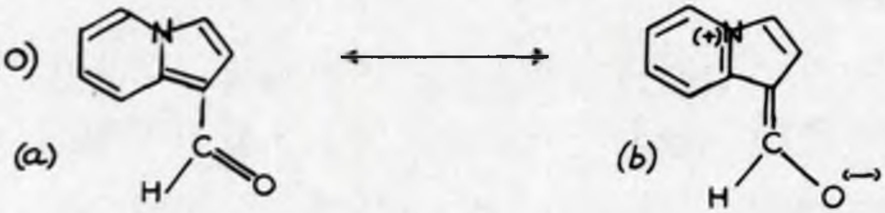
(a)
(b)

(19)



(a)
(b)

(20)



(a)
(b)

IV Indolizine Aldehydes

IV$_1$ The Synthesis of Indolizine Aldehydes.

Synthetic routes to 1(3)-formylindolizines, of which the Vilsmeier reaction is the most common, have been discussed in AV$_4$. It was expected that 3 (1)-ethoxymethyleneindolizinium salts, in analogy with the ethoxymethyleneazulenium salts,[122] would readily undergo hydrolysis to the corresponding 3(1)-formylindolizine. However ethoxymethyleneindolizinium perchlorates were found to be resistant to both neutral and alkaline hydrolysis. The following procedure was devised for their conversion to the corresponding aldehydes. Reaction of the ethoxymethyleneindolizinium perchlorate with a secondary amine afforded readily dialkyl- or alkyl-aryl aminomethyleneindolizinium perchlorates (16). The cations in these salts are identical with the cations formed in the Vilsmeier reaction with the corresponding indolizine and underwent alkaline hydrolysis to give the indolizine aldehyde. The reaction sequence is shown in Fig. 7 exemplifying the formation of 3-formyl-2-methylindolizine (17).

The methylphenyl- or diethyl- aminomethyleneindolizinium perchlorates, which correspond to the intermediates in the Vilsmeier reaction, could be isolated as blue or green dyes. More usually, however, reaction was performed by the addition of an excess diethylamine to the ethoxymethyleneindolizinium salt, after which the mixture was gently warmed, an excess of 10% ($^w/_v$) sodium hydroxide was added, and the resulting mixture was steam-distilled or refluxed to give in moderate to good yield the crude formyl indolizine. This was then purified by vacuum distillation or sublimation followed by recrystallisation.

The contrasting behaviour of ethoxymethyleneindolizinium and azulenium salts to hydrolysis would seem to indicate (i) that the contribution to the resonance hybrid of the structure in which the positive charge resides on the exocyclic carbon atom predominates to a greater extent with the ethoxymethyleneazulenium cation than the corresponding ethoxymethyleneindolizinium cation (ii) that the retention of the cationic structure rather than the formation of the neutralised molecule is favoured in the indolizine system. The cationic structure may be retained however and its stability enhanced, when diethylamine or N-methylaniline is condensed with 3(1)-ethoxymethyleneindolizinium perchlorate, since in the resulting aminomethyleneindolizinium perchlorate (Fig. 7 (16) a,b and c) resonance can occur between tertiary and quaternary nitrogen. The structure ((16)c) in which the positive charge is resident upon the exocyclic carbon atom attached directly to the nucleus must also participate to some extent in the resonance hybrid, since aminomethyleneindolizinium perchlorates undergo alkaline hydrolysis with the formation of the indolizine aldehyde.

IV_2 Investigation of the Polarisation of Indolizine Aldehydes by Infrared Spectral Studies.

Owing to the ready polarisation of the azulene nucleus interaction between the carbonyl group and the π-electrons of the nucleus is greater in 1-acylazulenes than in acylated benzenoid hydrocarbons. The carbonyl stretching frequency of 3(1)-formylazulenes (18) is reduced due to the important contribution of the dipolar form ((18)b) to the resonance hybrid in the ground state. The degree of polarisation depends on the substituents attached to the azulene nucleus,[126] and varies from 1646 cm^{-1} (nujol) for 1-formylazulene ((18), $R_1 = R_2 = R_3 = H$) to 1610 cm^{-1} (nujol) for 3-formylguaiazulene ((18) $R_1 = R_2 = Me, R_3 = Pr^i$) compared with 1700 cm^{-1} (CS_2) for 1-formylnapthalene and 1705 cm^{-1} (CS_2) for 6-formyl 4,8-dimethylazulene which are considered to be normal. The similarity of the structural features of indolizine and azulene suggests that 1(3)-formylindolizines should also show considerable polarisation of the carbonyl group due to the important contribution of structures of the type ((19) and (20)b). The stability and contribution of the structures ((19) and (20)b) affecting the polarisation of the carbonyl group, would similarly be anticipated to depend on the substituents attached to the indolizine nucleus. The carbonyl stretching frequency of the eleven 3(1)-formylindolizines prepared were measured in order to investigate a possible correlation between the degree of polarisation of the carbonyl group and the nature, number and position of substituents present in these aldehydes.

The infra-red carbonyl absorption frequencies of 3(1)formyl-indolizine are displaced from the positions of normal carbonyl absorption to regions which are more usually associated with carbon-carbon double bonds (1600 cm^{-1}). In order to identify the peaks in the region (1650 - 1610 cm^{-1}) with those caused by carbonyl absorption, the following procedure, which depends on the varying degree of polarisation of the carbonyl group[127] in solvents of differing polarity, was adopted.

The infra-red spectrum of a (0.05 molar) solution of the indolizine aldehyde was recorded in at least three of the following solvents, listed in order of increasing polarity; tetrachloroethylene (T.C.E.), carbon tetrachloride (CCl_4), tetrahydrofuran (T.H.F.), acetonitrile (CH_3CN), chloroform $CHCl_3$ and tetrabromoethane (T.B.E.). The effect of the solvents background absorption was minimised, using a double beam technique with an identical solvent cell. The peaks in the region (1660 - 1500 cm^{-1}) were measured manually, with an estimated error of $\pm$ 1 cm^{-1}. The peaks in the region (1650 - 1610 cm^{-1}) were strong and shifted along the frequency scale to a lower wavenumber with increase in solvent polarity, whereas those in the region (1610 - 1500 cm^{-1}) were weak and therefore were measured with solutions of higher concentration. The latter, lower absorption peaks showed little or no shift with change of solvent.

Thus the strong peaks in the region (1660 - 1610 cm^{-1}) can be attributed to carbonyl absorption.

1-Formylindolizines showed characteristic carbonyl absorption doublets. The main peak of the doublet occurred at higher wave-number in the less polar solvents whereas in chloroform and tetrabromoethane it occurred at lower wavenumber. The 3-formyl-indolizines on the other hand gave single peaks, with the exception of 2-phenylindolizine which gave twin peaks in tetrachloroethylene and carbon tetrachloride. According to the above observations it would appear that the condensation of 3-methyl-2-phenylindolizinium perchlorate with ethyl *ortho*formate occurs preferentially at the 1- position, possibly due to the combined *steric* effects of the methyl and phenyl groups resident on either side of the reactive 3- position.

A summary of the infra-red carbonyl stretching frequencies of the 3(1)-formylindolizines is listed in Table V. The values cited for 1-formylindolizines are the mean values for the doublet. Table VI records the difference between the carbonyl stretching frequencies (cm^{-1}) in the two limiting solvents. This difference is a measure of the relative polarizability of the 3(1)-formylindolizines.

TABLE V.

Carbonyl stretching frequencies (cm^{-1}) of 3(1)-Formylindolizines.

Indolizine Aldehyde	SOLVENT					
	T.C.E.	CCl_4	T.H.F.	CH_3CN	$CHCl_3$	T.B.E.
3-formyl-2 methyl	1639	1637	1636	1630	1626	1621
3-formyl -1,2-dimethyl	1638	1636	1635	1626	1616	1615
1-formyl -2,3-dimethyl	1644	1645	1642	1639	1635	1632
3-formyl -2,6-dimethyl	1640	1636	1638	1625	1621	1620
3-formyl -2,8-dimethyl	1642			1630	1624	1622
1-formyl- 3-ethyl-2-methyl	1645			1637	1635	1633
3-formyl 2-phenyl	1639	1630	1630	1627	1622	1620
3-formyl 1-methyl-2-phenyl	1637				1619	1615
3-formyl 2 methyl-1-phenyl	1637				1624	1620
1-formyl-3- methyl-2 phenyl	1645				1634	1632
(3)1-formyl-3- methyl-2-phenyl	1644				1637	1634

TABLE VI

Difference in carbonyl stretching frequencies (cm^{-1}) of 3(1)-formylindolizines in tetrachloroethylene and tetrabromoethane.

Indolizine Aldehyde	cm^{-1} T.C.E.	cm^{-1} T.B.E.	cm^{-1}
-3 formyl-2 methyl	1639	1621	18
-3 formyl-1,2-dimethyl-	1638	1613	25
-1-formyl-2,3-dimethyl-	1644	1632	12
3-formyl-2,6-dimethyl-	1640	1620	20
3-formyl-2,8-dimethyl	1642	1622	20
1-formyl-3-ethyl-2-methyl-	1643	1633	10
3-formyl-2-phenyl	1639	1620	19
3-formyl-1-methyl-2-phenyl-	1637	1615	22
3-formyl-2-methyl-1-phenyl-	1637	1620	17
1-formyl-3-methyl-2-phenyl	1643	1632	11
1(3)-formyl-5-methyl-2-phenyl	1644	1634	10

The following conclusions can be drawn (i) Taking the frequency observed in chloroform as a guide to the polarisation of the carbonyl bond, the order of decreasing polarisation is 3-formyl-1,2-dimethyl-

3-formyl-1-methyl-2-phenyl- > 3-formyl-2,6-dimethyl- > 3-formyl-2-phenyl- > 3-formyl-2,8-dimethyl- $\simeq$ 3-formyl-2-methyl-1-phenyl- > 3-formyl-2-methyl- > 1-formyl-

3-methyl-2-phenyl- $\simeq$ 1-formyl-3-methyl-2-methyl- $\simeq$ 1-formyl-2,3-dimethyl- $>$ 1-formyl-3-methyl-2-phenyl- indolizine.
(ii) The above order of decreasing polarisation is almost identical to the order of decreasing polarisability, the 3-formyl-2,8-dimethyl- and 3-formyl-2-phenyl-indolizines being interchanged. (iii) Both the polarisation and polarisability of 1-formyl indolizines are significantly lower than their 3-formyl isomers. The contribution of the dipolar structures of the type ((19)b) is thus inferred to be greater to the hybrid structure for 3-formylindolizines than the dipolar structure of the type ((20)b) is to the hybrid structure for 1-formylindolizines. (iv) Replacement of a 2-methyl group by a 2-phenyl group has little effect on the polarisation of the indolizine aldehyde. In contrast the replacement of a 1-methyl group in 3-formyl-1,2-dimethyl-indolizine results in a considerable reduction in the polarity and polarisability of the carbonyl bond.

XVI Reactions of Indolizines and Di-indolizinylmethanes with Triphenylmethyl Perchlorate.

The triphenylmethyl cation has recently found useful application as a dehydrogenating agent,[128,129,130] generally and most conveniently in the form of the perchlorate. In the first step of the dehydrogenation, hydrogen is abstracted as hydride ion from a suitable substrate (RH). Subsequent loss of a proton from an acidic site in the resulting carbonium ion (R^+) normally completes the dehydrogenation.

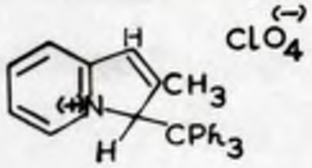
(1) $RH + Ph_3C^+ClO_4^- \longrightarrow R^+ \quad ClO_4^{(-)} + Ph_3CH$

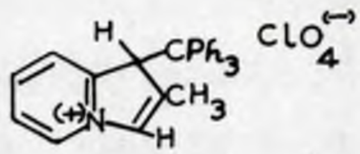
(2) $R^+ \longrightarrow$ Final product $+ H^+$

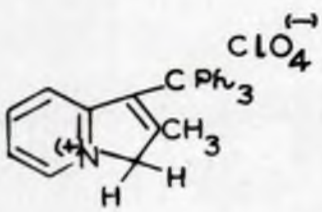
A prerequisite for step (1) to proceed is that the cation (R^+) formed should be relatively stable, when the structure of (R^+) is very stable with a resonance energy comparable or greater than that of the conjugate base (final dehydrogenation product) it becomes the actual product isolated. Thus when cycloheptatriene,[129] triphenylcyclopropene,[131] perinapthene[132] or a number of dihydroheteroaromatic structures[130] are dehydrogenated by triphenylmethyl perchlorate, hydride ion is abstracted from the substrate with isolation of the corresponding stable cations as their perchlorates.

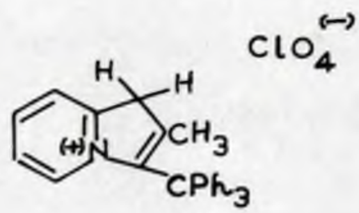
When indolizine is added to a solution of triphenylmethyl-perchlorate in acetonitrile, the colour of the triphenylmethyl perchlorate is discharged and a crystalline product isolated, which analysed for the substitution of two triphenylmethyl groups into the indolizine nucleus. Electrophilic substitution rather than hydride abstraction is thus

(21)

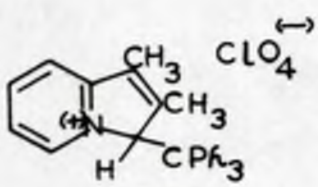
(A) 

(B.) 

(C.) 

(D.) 

(22)

(A.) 

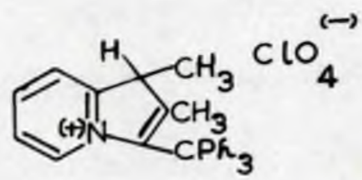
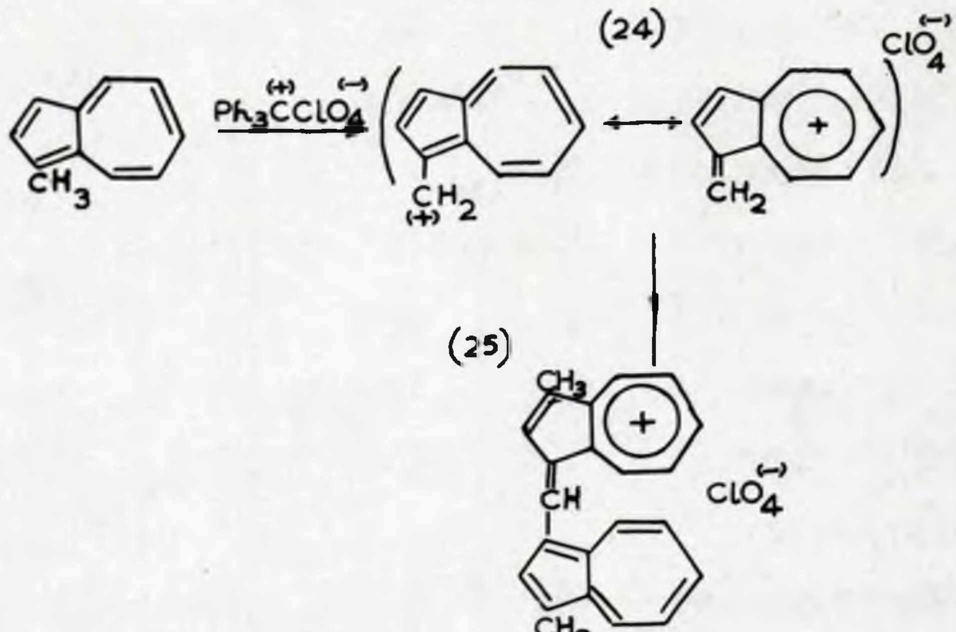
(B.) 

FIG. 8

(23) (24) (25)



the preferred process, presumably at the reactive 1- and 3- sites. This reaction has an almost exact parallel in the azulene series when a mixture of 1-triphenylmethylazulene and 1,3-bis-triphenylmethylazulene is obtained in the reaction of equivalent amounts of triphenylmethyl perchlorate and azulene.[136]

Reaction of triphenylmethyl perchlorate with 2-methyl- and 1,2-dimethyl-indolizine gave salts which on hydrolysis afforded triphenylmethyl-2-methyl- and -1,2-dimethylindolizines. Thus 2-methyl- and 1,2-dimethyl-indolizines undergo electrophilic attack by triphenylmethyl perchlorate without the subsequent elimination of a proton, the presence of the methyl groups increasing the stability of the resulting indolizinium cations. The addition products in the case of 2-methylindolizine, assuming attack at the reactive 3- or 1- positions, could be one or a mixture of the four isomers (21) A,B,C and D) and in the case of 1,2-dimethylindolizine one or a mixture of the two isomers ((22) A and B).

The proton magnetic resonance spectrum of the addition product from the reaction of triphenylmethyl perchlorate with 2-methylindolizine is shown in fig. m opposite page 89. The salient peaks are summarised in Table I. The spectrum consists of (i) a low-field group of signals in which a low-field doublet at δ 8.95 and a strong absorption signal whose main peak occurs at δ 7.37 are the most prominent features; (ii) two singlets at δ 5.65 and δ 1.79.

On the basis of comparison with the spectra (i,j,l) of 2-phenyl-

1-methyl-2-phenyl-, 1,3-dimethyl-2-phenyl-indolizinium perchlorates, the low-field doublet at δ 8.95 and the strong absorption peak at δ 7.37 are attributed to H-5 and to the three phenyl groups of the triphenyl methyl substituent, respectively (see Table I). The singlet at δ 5.63 from its spectral position and integral (equivalent to two protons), is likewise attributed to a C-3 methylene group (see Table I and spectra of salts (a,b,c,e,f,i and j). We conclude therefore that protonation occurs at the 3-position, and accordingly that the triphenylmethyl group has entered the 1-position of 2-methylindolizine. Isomer ((21)c) is the isolated addition product. It is interesting to note the upfield displacement of the signal of the 2-methyl group in this salt at δ 1.79 (c.f. δ 2.41 for 2-methyl-3*H*-indolizinium perchlorate). This is interpreted to arise from the increased shielding produced by the ring currents in the phenyl groups constituting the triphenylmethyl substituent. The stereochemistry of the cation may be such that no rotation of the triphenylmethyl C-1 bond takes place and the 2-methyl group is subjected to shielding by a single phenyl group, alternatively and more probably if rotation does occur the methyl group experiences an averaged shielding of all the possible configurations of the triphenylmethyl group with respect to the nucleus. A study of the spectrum over a temperature range would clarify this point.

The question of which isomer ((22) A or B) is isolated in reaction of triphenylmethyl perchlorate with 1,2-dimethylindolizine has still to be solved, but it may be tentatively suggested that structure ((22)B) is the more probable by virtue of the steric, inductive and hyperconjugative effects operating.

1,1',2,2'-Tetramethylmethylene-3,3'-di-indolizine (2) did not react cleanly with triphenylmethyl perchlorate, but the isolation of triphenylmethane in nearly quantitative yield suggests that hydride abstraction is the predominating process.

XVII Reaction of Indolizines and Di-indolizinylmethanes with High Potential Quinones and Examination of the Resulting Products.

XVII$_1$ Introduction

The dehydrogenation of carbocyclic[133] and heterocyclic[134,135] hydroaromatic compounds by quinones has been reported and evidence presented[133] that the former compounds are dehydrogenated by a two stage ionic process analogous to the mechanism by which triphenylmethyl perchlorate acts as a dehydrogenating agent. In the first and rate determining step (1), abstraction of hydrogen as hydride ion takes place and is followed by rapid proton transfer (2).

$$RH_2 + Q \xrightarrow{slow} RH^+ + QH^- \qquad (1)$$

$$RH^+ + QH^- \xrightarrow{fast} R + QH_2 \qquad (2)$$

When RH^+ is particularly stable, as discussed in the previous section (XVI), reaction may not proceed beyond the initial step (1), the cation (RH^+) being isolated as the quinolate or as the salt of an added acid.

XVII$_2$ Reaction of Indolizines with Quinones.

Both 2-methyl- and 1,2,-dimethyl-indolizine undergo electrophilic attack rather than hydride exchange with triphenylmethyl perchlorate with the formation of the corresponding triphenylmethylindolizinium perchlorate. In contrast the reaction of triphenylmethyl perchlorate with 1-methylazulene (23)[136] gave 1-(3-methylazulen-1-yl) methylene-3-methylazulenium perchlorate (25) whose formation is accounted for by preliminary hydride exchange of the substrate with the triphenylmethyl cation to give the methyleneazulenium perchlorate (24). The reaction is outlined in Fig. 8. It would appear therefore that the greater charge density associated with the 1- and 3- positions of the indolizine nucleus favours electrophilic attack, with subsequent formation of the indolizinium salt, to hydride abstraction from the methyl substituents.

It was hoped that by using high potential quinones for hydride abstraction an analogous reaction to that given by 1-methylazulene with triphenylmethyl perchlorate might ensue. A 20% yield of the quinol resulted when 2,3-dimethylindolizine and 2,3,5,6 tetrachloro-1,4-benzoquinone were allowed to react. The isolation of quinol implies that hydride abstraction occurs to some extent, but the reaction is possibly complicated by condensation of the quinone[137] at the vacant C-1 site. Reaction of the same quinone with 1,2,3-trimethylindolizine in the cold gave the quinol in 82% yield. The products of the reactions other than the quinol were uncharacterisable and require further study.

$BVII_3$ Reaction of Di-indolizinylmethanes with Quinones.

The failure of triphenylmethyl perchlorate to yield a characterisable product in the dehydrogenation of 1,1'2,2'-tetramethylmethylene-33'-di-indolizine (2) prompted the use of high potential quinones. Simple abstraction of hydride ion from the methylene group, using various di-indolizinyl methanes as substrate in methanol with the subsequent addition of perchloric acid to give the corresponding monomethine dye salt (12), occurred only with 1,1',2,2'-tetramethylmethylene-3,3'-di-indolizine. Even so, the production of the blue (1,2-dimethylindolizin-3-yl) methylene 1,2-dimethylindolizinium perchlorate (12) was accompanied by the formation of a sparingly soluble green crystalline salt. The yield of both the blue monomethine dye salt (12) and this green salt, whose structure is discussed in (BVII$_4$ and BVII$_5$), slightly increased with increase in reaction time from 2-15 minutes. The yield of green salt is greatly increased if the reactionis carried out in acetonitrile in place of methanol as solvent. However, in acetonitrile a pure sample of the monomethine dye salt is not isolated. The green salt is isolated in fair yield using 2,3,5,6- and 3,4,5,6- tetrachloro-1,4- and -1,2- benzoquinone, and in poorer yield using 2,3-dicyano- or 2,3,-dichloro-5,6-dicyano-1,4-benzoquinone.

In view of the interesting results obtained with quinone dehydrogenations on 1,1',2,2'-tetramethylmethylene-3,3'-di-indolizine the reaction of 2,3,5,6- and 3,4,5,6- tetrachloro-1,4- and -1,2- benzoquinones was also attempted with the following methenes, 2,2'-dimethylmethylene-3,3'-di-indolizine(1), 1,2,2'-trimethyl-methylene-3,3'-di-indolizine (6), 2,2',3,3'-tetramethylmethylene-1,1'-di-indolizine (4), and 2,2'-dimethyl-1,1'-diphenylmethylene-3,3'-di-indolizine (3), using both methanol and acetonitrile as solvents. However singularly disappointing results were obtained as neither compounds corresponding to the green salt obtained from 1,1',2,2'-

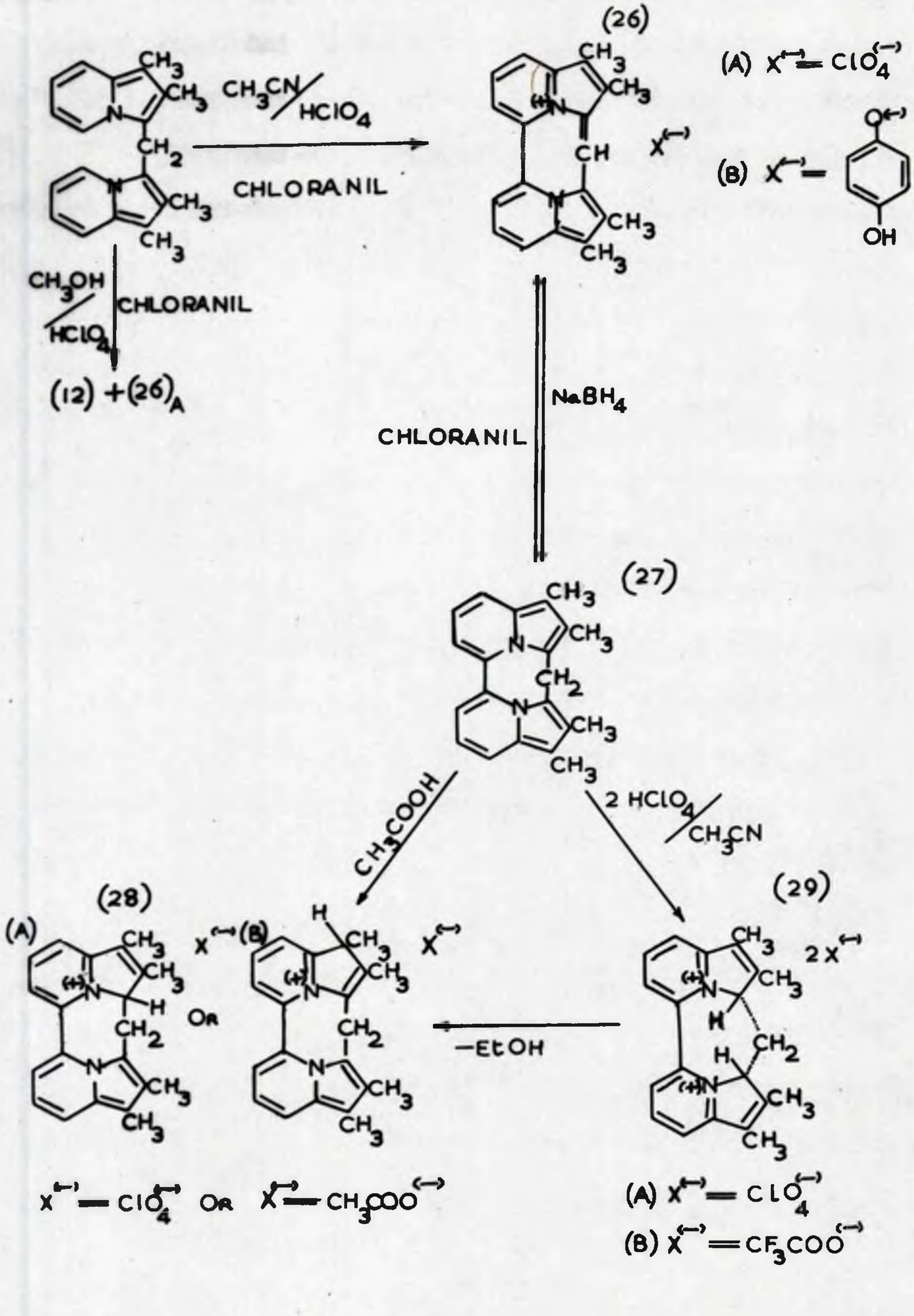
tetramethylmethylene-3,3'-di-indolizine (2), nor pure samples of the corresponding monomethine dye salts could be isolated.

$BVII_4$ Structure and Reactions of the 'Green Salt' (26) Isolated from the Quinone Dehydrogenations of 1,1',2,2'-tetramethyl-methylene-3,3'-di-indolizine.

The visible absorption spectrum of the green salt (Plate II) in which significant log E values persist to wavelengths greater than 900 mμ suggested an unusual type of structure for this compound. The following reactions were undertaken to aid in the elucidation of its structure. Analysis of the green salt suggested the elimination of two hydrogens less than that of the monomethine dye salt (12). Sodium borohydride reduction of the green salt gave a red base, soluble in ether, benzene and chloroform, whose analysis indicated the loss of two hydrogen atoms from the methane (2) and which underwent hydride-abstraction with chloranil in the presence of perchloric acid to regenerate the green dye salt. The red base formed a colourless diperchlorate in acetonitrile containing an excess of perchloric acid, which underwent solvolysis to a purple monoperchlorate in ethanol. The red base was not reduced by hydrogenation over palladium on charcoal catalyst. The spectra of the red base and the monoperchlorate are also shown on plate II .

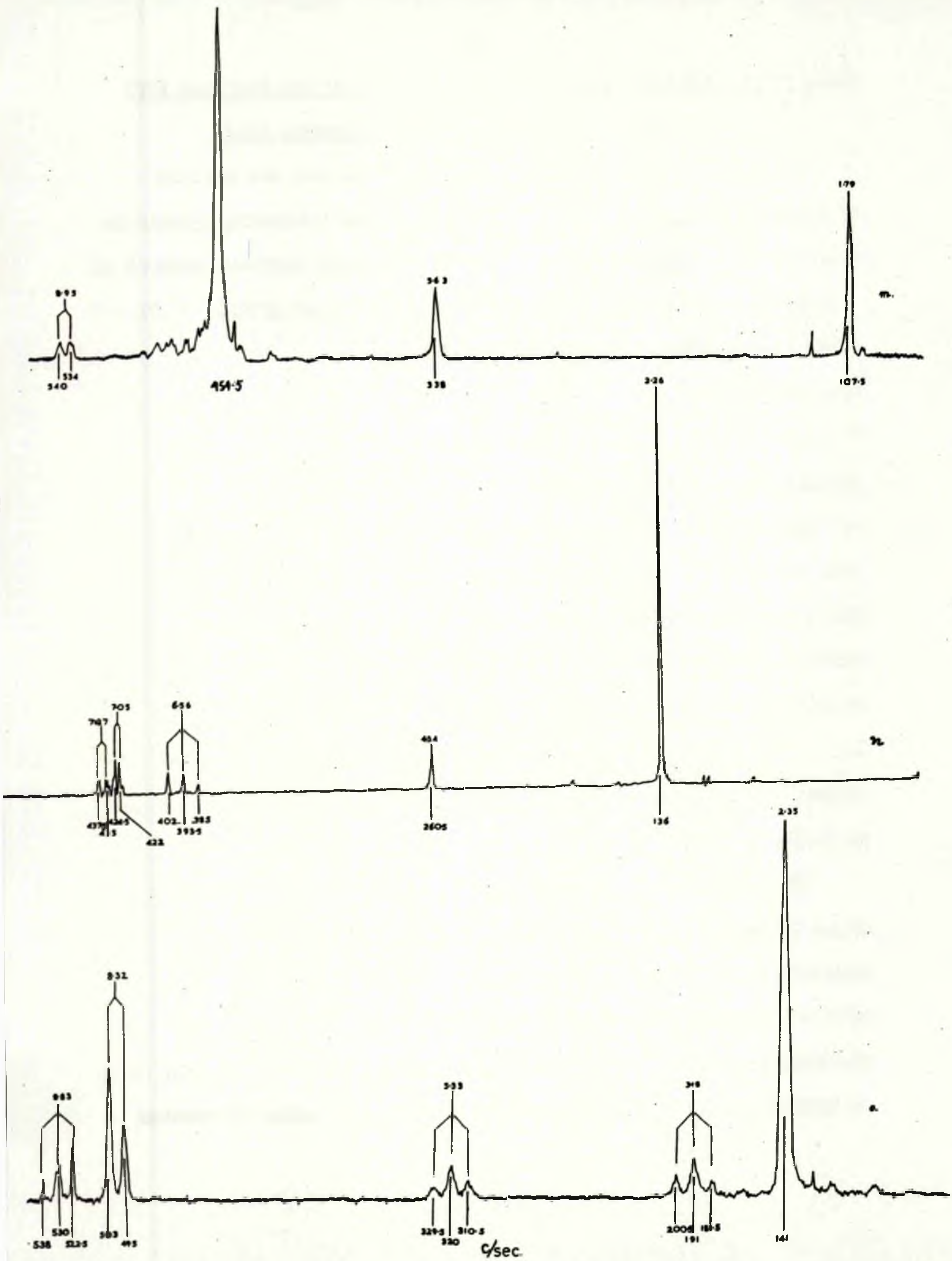
The proton magnetic resonance spectra of the red base in deuterochloroform and trifluoracetic acid were recorded (Fig. n and o respectively). The structures of the green salt (26A) and the

FIG.9



related red base (27), and the monoperchlorate (28) and diperchlorate (29), whose nomenclatures are formally given as 4,5,7,8 - tetramethyl- [1,4] -diazepinodi [7,1,2-cd : 5,4,3-c'd'] indolizin-12-ium perchlorate, 4,5,7,8-tetramethyl-6H- [1,4] -diazepinodi [7,1,2-cd: 5,4,3-c'd'] indolizine, 5a,6-dihydro-4,5,7,8-tetramethyl- [1,4] - diazepinodi [7,1,2- cd: 5,4,3-c'd'] indolizin-12-ium and 6,6a-dihydro -4,5,6,8-tetramethyl-5aH- [1,4] -diazepinodi [7,1,2-cd: 5,4,3-c'd'] indolizindi-ium diperchlorate respectively, accommodate all the chemical and spectral findings and are shown in Fig. 9 The structure of the monoperchlorate (28) could be either ((28)A) or ((28)B) of which structure ((28)B) would minimise the distortion and so allow more effective conjugation between the seven and five-membered rings. Unfortunately the proton magnetic resonance spectrum of the monoperchlorate, which would clarify this point has yet to be recorded.

A mechanism by which the methane (2) is converted into the green salt ((26)A) by reaction with quinone is difficult to envisage. It is difficult at present to explain why of all the methanes (1) (2) (3) (4) and (6), (2) is the only one to yield the diazepino type of compound and why the yield of this compound is better in acetonitrile rather than methanol as solvent There is spectral evidence that the quinolate ((26)B), which can be isolated as a brown amphorous solid, is the product of reaction of chloranil with 1,1',2,2'-tetramethyl-methylene-3,3'-di-indolizine in the absence of perchloric acid.


m.
540
534
454·5
338
1·79
107·5
2·26
7·05
6·56
n.
402
393·5
385
422
2605
136
2·35
8·32
538
530
522·5
503
495
329·5
320
310·5
200·5
191
181·5
141
o.
c/sec

BVII$_5$ The Proton Magnetic Resonance Spectra of the Red Base (27) in Deuterochloroform and Trifluoroacetic Acid.

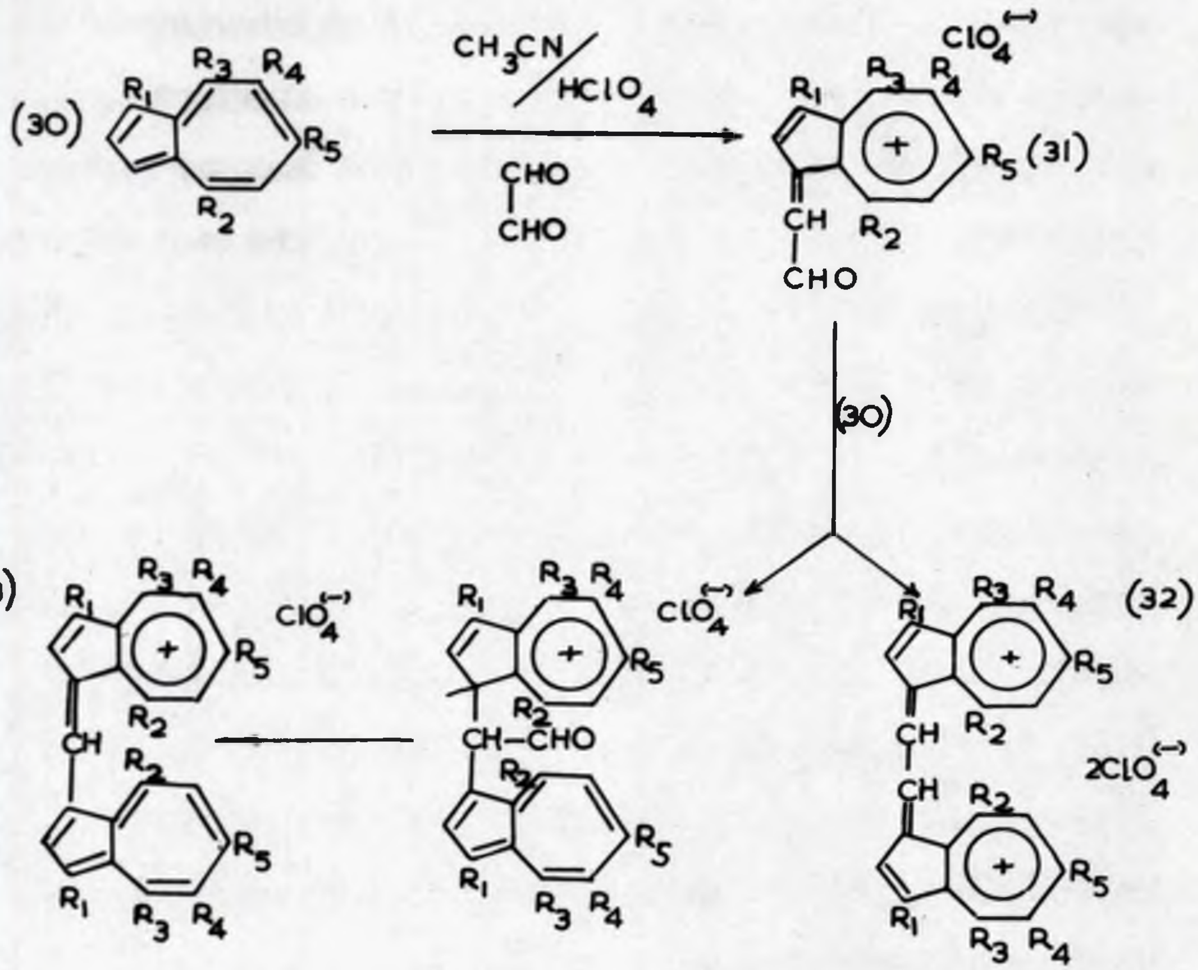
The proton magnetic resonance spectrum of the red base in deuterochloroform (Fig. n) is comprised of the following signals in order of decreasing δ values. (i) Two low field doublets centred at δ 7.27 and δ 7.03, (ii) a triplet with geometrical centre δ 6.56 and (iii) two singlets, the weaker of which occurs at δ 4.34 and the stronger at higher field δ 2.26. Integration of the spectrum shows the ratios of the intensities of these peaks to be 1:1:1:1:6, respectively. This suggests the number of protons to be a multiple of ten and taking this in conjunction with the analytical data of the red base and the nature of the starting material (methane (2)) suggests the compound to contain twenty protons. The signals therefore correspond to 2,2,2,2 and 12 protons, respectively. The twelve proton signal at δ 2.26 can be attributed to four methyl groups in the 1,1',2 and 2' positions of the indolizine nuclei, and the 2 proton signal at δ 4.34 to the protons of the 3,3'-methylene group on the basis of their spectral positions and lack of multiplicity.

The remaining signals must be due to 6 protons in the pyridine rings of the indolizine nuclei. The simplicity of the spectrum suggests elimination of equivalent protons from the indolizine nuclei with the formation of a symmetrical five ring structure. The two doublets have identical splittings but the symmetry is not that of an AB system hence the doublets must arise from two pairs of protons each member of each pair being coupled to a single proton. This third proton is responsible for the triplet at δ6.56 due to coupling with two adjacent near equivalent protons. Hence the molecule must contain three adjacent protons in each pyridine ring. This could only be accounted for by 5 5' or 8 8' bridging and the latter can be eliminated on a stereochemical basis. The structure of the red base is thus concluded to be (27).

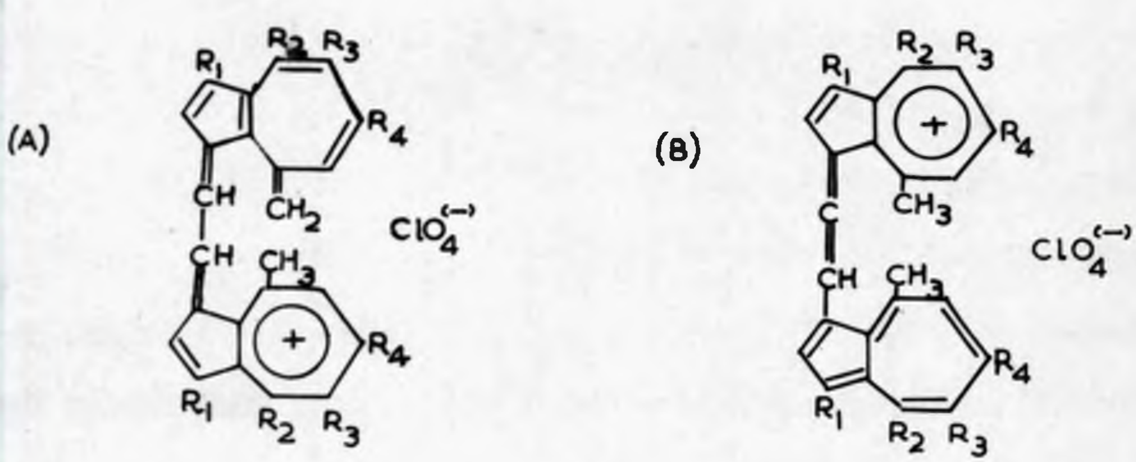
Further evidence that the red base possesses the structure (27) is provided by a study of the proton magnetic resonance spectrum of the red base in trifluoroacetic acid (Fig. O.). The spectrum consists of the following signals in order of decreasing δ values: (i) A low field triplet centred at δ 8.83, (ii) a doublet at δ 8.32, (iii) a triplet at δ3.35 (J = 9.5c./sec), (iv) a triplet at δ 5.18 (J = 9.5 c./sec), (v) a singlet at δ2.35.

Integration of the spectrum shows the ratio of these signals to be 1:2:1:1:6 respectively and the signals are deduced to correspond to 2,4, 2,2 and 12 protons. The twelve-proton signal at δ 2.35 is attributed to four methyl groups at the 1,1',2 and 2' positions of the indolizine nuclei. Its spectral position is shifted slightly down-field with respect to the corresponding signal in Fig. n, and compares with the 1 and 2- methyl signals in (c), due to the presence of positively charged rather than neutral nitrogen. From a comparison of the spectrum (o) with that of 1,2-dimethylindolizinium perchlorate (c) the two-proton signal at δ 5.35 is attributed to the presence of a pair of substituted C-3 methylene protons. The multiplicity arises from spin-spin coupling to the bridging methylene group which is responsible for the triplet centred at δ 3.18. This deduction is confirmed by the identical splitting (J = 9.5 c./sec) of the two triplet signals. The low-field triplet equivalent to two protons is attributed to the pair of protons at position -7, the multiplicity arises from spin-spin coupling with the adjacent, near equivalent H-6 and H-8. The doublet at δ 8.32 equivalent to four protons is attributed to the identical chemical shift and splitting of the H-6 and H-8 pair of protons signal by that of H-7. The simplicity of the proton magnetic resonance spectrum of the red base in trifluoroacetic acid necessitates that diprotonation of the symmetrical structure of the red base also produces a symmetrical structure in which both the added protons reside on the same side of the central diazipine ring. The structure for the red base in trifluoroacetic acid is thus concluded to be ((29)B).

FIG.10



(34)

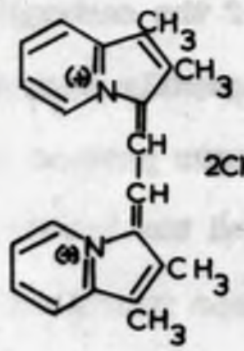


XVIII Condensation of Indolizinium Perchlorates with Glyoxal.

The anticipated similarity of azulene and indolizine has been referred to in Part A. The analogous chemical behaviour of the two systems is portrayed very strikingly in their condensation reactions with glyoxal and it is by virtue of this fact that the products of condensation with glyoxal for the two systems have been deduced.

The condensations of glyoxal in the presence of perchloric acid with azulene ((30) $R_1 = R_2 = R_3 = R_4 = R_5 = H$), 1-methylazulene (25), 4,6,8-trimethylazulene ((30) $R_1 = R_4 = H$ $R_2 = R_3 = R_5 = Me$) and guiazulene ((30) $R_1 = R_2 = Me$, $R_3 = R_5 = H$, $R_4 = Pr^i$) were initially investigated.[158] It was found that azulene and 1-methylazulene reacted to give the 1,1'-azulenylmethyleneazulenium perchlorates ((33) $R_1 = R_2 = R_3 = R_4 = R_5 = H$) and (26), respectively. On the other hand 4,6,8-trimethylazulene and guiazulene condensed in acetonitrile at both aldehyde functions to give ethanediylidene-bis-(4,6,8-trimethylazulenium perchlorate) ((32) $R_2 = R_3 = R_5 = Me$, $R_1 = R_4 = H$) and ethanediylidenebis-(5-isopropyl-3,8-dimethylazulenium perchlorate) ((32) $R_1 = R_2 = Me$, $R_3 = R_5 = H$, $R_4 = Pr^i$), respectively. The first step in the reaction mechanism is postulated to be common in all four condensations and results in the formation of a corresponding 1-formylmethyleneazulenium perchlorate (31). The difference in behaviour of the two highly alkylated azulenes compared with the parent compound and 1-methylazulene is then attributed to the accumulated electron - releasing effect of the alkyl groups, which lowers the

(35)



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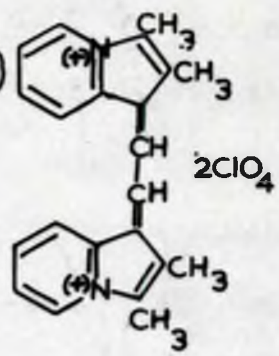

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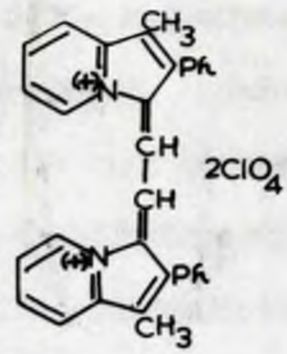

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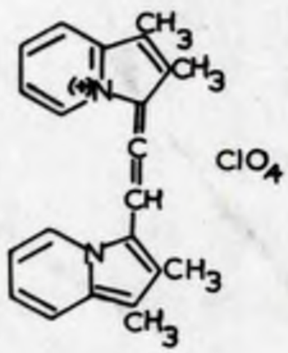

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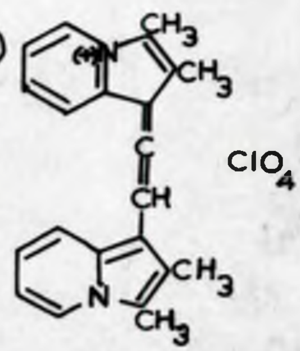

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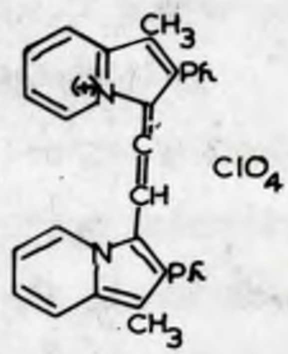

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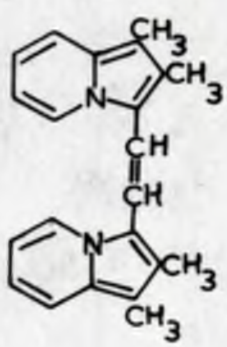

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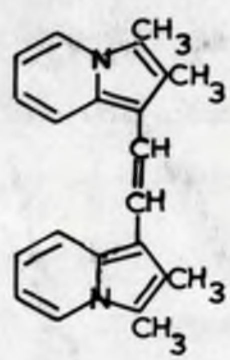

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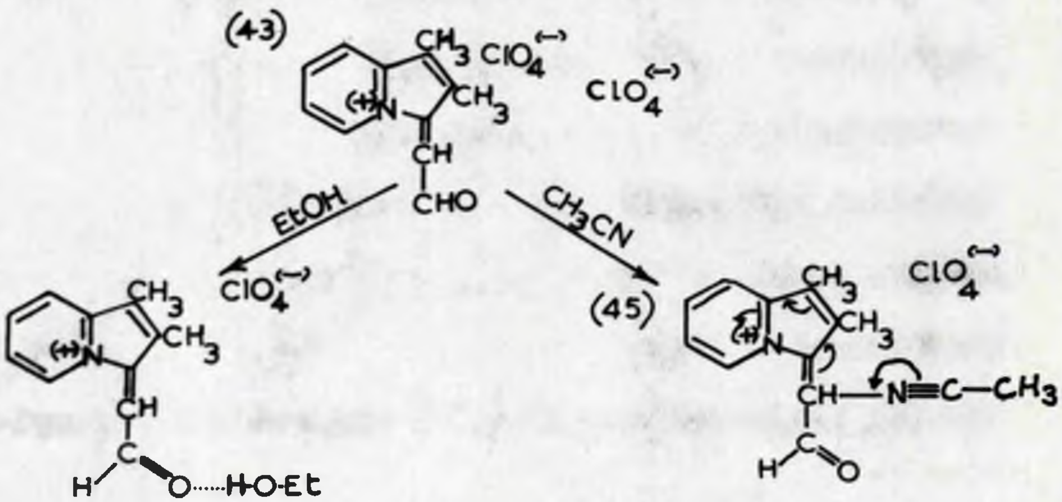

electrophilic nature of the methine carbon atom of the 1-formylazulenium perchlorate to a level below that of the carbonyl carbon atom. Attack of the unreacted azulene consequently occurs at the carbonyl rather than the methine carbon atom. The former process leads to ethanediylidenebis-(azulenium perchlorates) and the latter to azulenylmethyleneazulenium perchlorates. These reactions are summarised in Fig. 10.

It was subsequently found that the ethanediylidenebis-(azulenium perchlorates) lose a molecule of perchloric acid on attempted recrystallisation to give a monoperchlorate.[150] A possible structure of the type ((34)A $R_1=R_3=H$, $R_2=R_4=Me$) may arise, in the case of ethanediylidenebis-(4,6,8-trimethylazulenium perchlorate) ((32) $R_2=R_3=R_5=Me$, $R_1=R_4=H$), by proton loss from the acidic 4,6 or 8 methyl groups,[106] the acidity of which would be increased by the cationic charge present in the diperchlorates. Alternatively a proton may be lost from one of the methine carbon atoms to give the allene structure ((34)B $R_1=R_3=H$, $R_2=R_4=Me$).

1,2-Dimethyl-, 2,3-dimethyl- and 1-methyl-2-phenyl-indolizinium perchlorates condensed in the presence of excess perchloric acid using acetonitrile as solvent to give the corresponding ethanediylidenebis-(indolizinium perchlorates) (35) (36) (37). In analogy to the azulene series and the failure of 3H-1,2,3-trimethylindolizinium perchlorate to react with glyoxal, condensation of 1,2-dimethyl-(7A (c)) 2,3-dimethyl- (7 (g)) and 1-methyl-2-phenyl-(7A (j)) indolizinium perchlorates with glyoxal is deduced to occur at the reactive and vacant 3-or 1-positions. The indolizinium perchlorates (7A (e)), (7 (g)) and (7A (j)) condensed with glyoxal in ethanol to give in good yield monoperchlorates corresponding to (38), (39) and (40). The formation of the monoperchlorates from the condensation of 1,2-dimethylindolizinium perchlorate and glyoxal was accompanied by a small yield (5.5%) of (1,2-dimethylindolizin-3-yl) methylene -1,2-dimethylindolizinium perchlorate (12). The formation of the monomethine dye salt (12) and the ethanediylidenebis-(indolizinium perchlorate) is postulated to occur by a mechanism analogous to that suggested for the formation of the 1,1'-azulenylmethyleneazulenium perchlorates and the ethanediylidenebis- (azulenium perchlorates). Formation of the small percentage of the monomethine dye-salt (12) isolated only in ethanol solution, and not in acetonitrile, is ascribed to molecules of ethanol shielding the carbonyl group of the 1-formylmethyleneindolizinium perchlorate (43) by the formation of a hydrogen bridge. as shown in (44), and thus increasing the relative electrophilic activity of the methine carbon atom. Further, it is possible that the acetonitrile may reduce the electrophilic activity of the methine carbon atom by weak carbon-nitrogen interaction as depicted in (45), so that in this solvent the carbonyl carbon atom is the exclusive site for further condensation. When the condensation is carried out in ethanol the greater basicity of this solvent removes a proton from the most acidic site of the first formed ethanediylidenebis-(indolizinium perchlorates) (35) (36) and (37) with the resulting formation of the sparingly soluble monoperchlorates (38), (39) and (40). The absence of an acidic methyl group in the three indolizinium perchlorates studied limits the position of proton loss in the diperchlorates (35), (36) and (37) to one of the equivalent methine carbon atoms of the ethanediylidene bridge. The structures of the monoperchlorates from the diperchlorates (35), (36) and (37) are therefore 1,2-dimethyl-3-(1,2-dimethylindolizin-3-ylvinylidene) indolizinium perchlorate (38), 2,3-dimethyl-1-(2,3-dimethylindolizin-1-ylvinylidene) indolizinium perchlorate (39), and 1-methyl-2-phenyl-3-(1-methyl-2-phenylindolizin-3-ylvinylidene) indolizinium perchlorate (40), respectively. The visible absorption spectra of ethanediylidene-bis-(1,2-dimethylindolizinium perchlorate), ethanediylidenebis-(2,3-dimethylindolizinium perchlorate) and the corresponding monoperchlorates are shown on plate III

Sodium borohydride reduction in ethanol of the monoperchlorates (38) and (39) produced 1,1',2,2'-tetramethyl-trans-vinylene-3,3'-di-indolizine (41) and 2,2',3,3'-tetramethyl-trans-vinylene-1,1'-di-indolizine (42), respectively. The reduction product in both cases was a mixture of the cis- and trans- isomers. The more unstable isomer, assumed to be the cis- isomer, was destroyed by chromatographing the mixture on an alumina column. The stable trans- isomer was isolated as large orange needles which darkened slowly on exposure to light and air.

The tetramethylvinylene-di-indolizines (41) and (42) regenerated the corresponding diperchlorates (35) and (36) when brought into reaction with quinones in the presence of perchloric acid. Hydrogen is abstracted as hydride ion with the transitory formation of the corresponding monoperchlorates (38) and (39) which in the presence of excess perchloric acid are converted into the diperchlorates. The possibility of reversible protonation, leading to the diperchlorates (35) and (36) and of hydride transfer, leading to the formation of tetramethylvinylene- di-indolizines (41) and (42) from the mono-perchlorates (38) and (39) completely justifies the structures attributed to these compounds. The closely analogous characteristics of these condensation reactions of glyoxal with azulenes and indolizines, and the similarity of the resulting products, provide good evidence for the allene structures ((34)B $R_2 = R_4 = Me$, $R_1 = R_3 = H$) and ((34)B $R_1 = Me$, $R_2 = R_4 = H$, $R_3 = Pr^i$) for the monoperchlorates formed by proton loss from ethanediylidenebis-(azulenium perchlorates) ((52) $R_2 = R_3 = R_5 = Me$, $R_1 = R_4 = H$) and ((52) $R_1 = R_2 = Me$ $R_3 = R_5 = H$, $R_4 = Pr^i$), respectively.

PART C

Introductory Notes.

Melting points were determined on a Kofler-type heating stage. When the words 'preheated block' are used this implies that the heating block was heated to the cited temperature before the sample was placed on the block.

Visible spectra were measured or recorded with Unicam S.P.600 or S.P. 700 instruments. The wavelengths of the absorption maxima are given in mμ followed (in parenthesis) by intensities of absorption in $\log_{10}\varepsilon$ units.

Infra red spectra were recorded with a Grubb-Parsons Type G.S.2A instrument.

Nuclear magnetic resonance spectra were recorded with a Varian A-60 spectrometer operating at 60 megacycles per sec., at a sweep rate of 1 cycle per sec. per sec. The intensities of the signals were measured by the built-in integrator. Tetramethylsilane was used as the internal reference. Chemical shifts are given on the δ-scale, the absolute values being accurate to ± 0.015 p.p.m. on the precalibrated 500 c./sec. scale. J values were measured on the 500 c./sec. scale and are accurate to ± 0.3 c./sec. Signal positions quoted in c./sec. are down field relative to the tetramethylsilane line. The values were independent of concentration in the range 5-15% (w/v).

Micro-analysis were performed by Drs. Weiler and Strauss, Oxford. Samples for analysis were dried for 4-6 hours at 60 - 80°/0.1 m.m.

Samples dried in vacuo, were dried over potassium hydroxide and phosphoric anhydride.

Perchloric acid refers to 70-72% (w/w), analar grade, unless otherwise stated.

Chromatography was on activated alumina, Spence Type H, 100/200 mesh.

CI Preparation of Indolizines and Di-indolizinylmethanes.

CI_1 Indolizine. was prepared by the method of Boekelhide and Windgassen.[20] Redistilled 3-(2'-pyridyl)-1-propanol (20.0 g) and 10% palladium on charcoal (0.80 g) yielded indolizine (6.52 g, 37%), m.p. 73-74°, (lit. yield 50%; m.p. 73-74°).

CI_2 2-Methylindolizine was prepared (a) by the method of Borrows, Holland and Kenyon[6] in 46% yield, m.p. 58 - 58.5°, (lit. yield 49%; m.p. 57-59°). (b) By the method of Holland and Naylor[5] in 74% yield, m.p. 58.5-59°, (lit. yield 80%; m.p. 59°).

In the experimental work described in this section of the thesis the term "the extract from the steam distillate was worked up in the usual manner" has the following meaning: The ether extract of the steam-distillate was washed with hydrochloric acid (200 ml, 0.005 N), with water, dried (K_2CO_3) and the ether evaporated. The crude indolizine was then distilled at reduced pressure.

CI_3 1,2-Dimethylindolizine was prepared by the method of Holland and Naylor[5] in 69% yield, m.p. 59.5-60° (lit. yield 75%; m.p. 65°).

CI_4 2,3-Dimethylindolizine

a) By Tschitschibabin synthesis from 2-picoline and 3-bromobutan-2-one

3-Bromobutan-2-one (30.1g, 0.2 mole) was added to 2-picoline (18.60g, 0.2 mole). After the resulting mixture had been left to stand overnight white crystals of the quaternary salt had formed together with a thick green oil. The mixture was heated on a steam bath for

2 hours and then taken up in hot water and shaken with ether to remove unchanged reactants. After the addition of sodium hydrogen carbonate (35 g) to the aqueous solution of the quaternary salt, the resulting solution was steam-distilled to give cream coloured waxy crystals of product. The ether extract of the steam-distillate was worked up in the usual manner giving 2,3-dimethylindolizine (20.70 g; 72%), m.p. 55-56°. Tsuda and Ochai[140] reported a yield of 37%, m.p. 53-56° and Holland and Nayler[5] reported a yield of 61%, m.p. 37°; both groups of workers using slightly different modifications of the Tschitschibabin synthetic route.

b) <u>By the reduction of 3-formyl-2-methylindolizine with lithium aluminium hydride in the presence of Aluminium Chloride</u>.

Lithium aluminium hydride (2.08 g.) was added to aluminium chloride (18.8 g.) in dry ether (150 mls). After the reaction had subsided a solution of 3-formyl-2-methylindolizine (6.35 g) in dry ether (50 mls) was added during 5-10 minutes. The addition was accompanied by a vigorous reaction and the development of a transient orange colour. The mixture was then refluxed for 1 hour, allowed to cool, and carefully poured into an equal volume of ice-cold water. A little dilute sulphuric acid was added dropwise to clarify the aqueous layer. The ether extract was washed well with water and dried (K_2CO_3). Evaporation of the ether left the crude 2,3-dimethylindolizine as a yellow-brown oil which solidified on standing. This was distilled at 10 m.m. (block temperature 150°) to give pure

2,3-dimethylindolizine (1.38 g, 38%), colourless waxy plates, m.p. 38.5 - 41.5°. Rossiter and Saxon reported the lithium aluminium hydride reduction of 3-formyl-2-methylindolizine,[112] (10%; m.p. 39.5 - 40.5°).

CI$_5$ 2,6-Dimethylindolizine

A solution of 2,5-lutidine (22.6 mls, 0.2 mole) and bromoacetone[141] (27.4 g, 0.2 mole) in acetone (20 mls) was allowed to stand at room temperature. After approximately four minutes a vigorous reaction set in, causing the solution to reflux. Boiling was continued for 20 minutes by the application of external heating. The yellow precipitate of 1-acetonyl-2,5-dimethylpyridinium bromide (37.7 g, 77.3%) was filtered from the cooled mixture and washed with a little acetone. A specimen recrystallised from ethanol as colourless crystals, m.p. 196 - 198.5°.

Found N = 5.44. $C_{10}H_{14}BrNO$ requires N = 5.74

A solution of 1-acetonyl-2,5-dimethylpyridinium bromide (35.0 g.) and sodium hydrogen carbonate (35.0 g.) in water (300 mls) was boiled, and the resulting 2,6-dimethylindolizine was distilled in steam. The steam-distillate was dissolved in ether, and the extract was worked up in the usual manner to give 2,6-dimethylindolizine (14.7 g, 70%) as colourless waxy plates, m.p. 72.5 - 74.5°.

Found C = 82.86 H = 7.22 N = 9.65

$C_{10}H_{11}N$ requires C = 82.72 H = 7.64 N = 10.02

CI_6 2,8-Dimethylindolizine.

A solution of 2,3-lutidine (17.3 mls, 0.15 mole) and bromoacetone (20.55 g, 0.15 mole) in acetone (20 mls) was gently refluxed until the reaction mixture turned cloudy. Continued gentle heating brought about the formation of a light brown oil which yielded white deliquescent crystals of 1-acetonyl-23-dimethylpyridinium bromide (25.04 g, 68%) on scratching. A specimen crystallised from ethanol as colourless crystals which decompose > 232° with charring > 247°

Found N = 5.63 $C_{10}H_{14}BrNO$ required N = 5.74

A solution of 1-acetonyl-2,3,-dimethylpyridinium bromide (24.4 g, 0.1 mole) and sodium hydrogen carbonate (25 g) in water (300 mls) was boiled and the resulting 2,8-dimethylindolizine distilled in steam. The distillate, a yellow oil, on being worked up in the usual manner gave 2,8-dimethylindolizine (4.32 g, 30%), b.p. 121°/20 mm

Found N = 9.56 $C_{10}H_{11}N$ requires N = 9.65

CI_7 3-Ethyl-2-methylindolizine was prepared in 72% yield, b.p. 125°/15 mm, by the method of Borrows, Holland and Kenyon,[4] (lit. yield 67%; b.p. 134°/15 mm).

CI_8 1,2,3-Trimethylindolizine was prepared (a) By the method of Rossiter and Saxton[112] in 60% yield b.p. 134-136°/10 mm. (lit. yield 67%; b.p. 85-87°/0.095 mm.)

(b) By the Reduction of 3-formyl-1,2-dimethylindolizine with lithium aluminium hydride.

A solution of 3-formyl-1,2-dimethylindolizine (2 g) in dry ether

(200 mls) was added over 30minutes to a solution of lithium aluminium hydride (2g) in dry ether (200 mls). The resulting mixture was refluxed for 2½ hours and then allowed to stand at room temperature for 40 hours. The solution was slowly poured into ice-cold water (400 mls), and a little dilute sulphuric acid was added dropwise to clarify the aqueous layer. The ether extract was washed free from acid with water and dried (K_2CO_3). Evaporation of the ether afforded the crude 1,2,3-trimethylindolizine as a yellow-brown oil. Distillation at 12 mm (block temperature 142°) yielded 1,2,3-trimethylindolizine (1.04 g, 58%) as a yellow oil.

CI_9 2-Phenylindolizine was prepared by the method of Borrows, Holland and Kenyon.[6] 2-Methyl-1-phenacylpyridinium bromide, m.p. 215°(d) was obtained in 60% yield (lit. yield 75%; m.p. 215°(d)). This salt gave 2-phenylindolizine (93%), m.p. 214.5° (d), (lit. yield 96%; m.p. 215°(d)).

CI_{10} 1-Methyl-2-phenylindolizine.

2-Ethylpyridine (11.3 mls, 0.1 mole) was added to a solution of phenacyl bromide[142] (19.9 g, 0.1 mole) in ethanol (25 mls) and the resulting solution was refluxed for 30 minutes. Addition of ether to the cold solution gave a white precipitate of 2-ethyl-1-phenacylpyridinium bromide (25.57 g, 83%) which was filtered, washed with a small volume of ethanol and with much ether. A specimen recrystallised from ethanol as colourless crystals, m.p. 179 - 181°.

Found N = 4.32 $C_{15}H_{16}BrNO$ requires N = 4.57

A solution of 2-ethyl-1-phenacylpyridinium bromide (9.16 g, 0.03 mole) and sodium hydrogen carbonate (10 g) in water (100 mls) was refluxed for 30minutes. 1-methyl-2-phenylindolizine separated out as a brown oil which solidified on cooling to light brown needles. These were collected and the filtrate was boiled again to yield a further quantity of product. The combined crops (6.028 g, 97%) were washed with water, dried in vacuo and recrystallised from ethanol giving 1-methyl-2-phenylindolizine as cream coloured needles, m.p.85 - 86°.

Found C = 86.5 H = 6.45 N = 6.75

$C_{15}H_{13}N$ requires C = 86.92 H = 6.32 N = 6.76

CI$_{11}$ 2-Methyl-1-phenylindolizine

2-Benzylpyridine (24 mls, 0.15 mole) was added to bromoacetone (12.6 mls, 0.15 mole). A vigorous reaction set in almost immediately to give a dark brown oil which was heated on a steam bath for 4 hours, then taken up in water. The aqueous solution was extracted several times with chloroform. Sodium hydrogen carbonate (20 g) was added and the resulting mixture refluxed for 1½ hours. A dark brown oil separated out. The mixture was extracted several times with ether, and the ether extracts were washed with dilute hydrochloric acid (200 mls, 0.00 5 N), and water, before being dried (K_2CO_3). The ether was evaporated and the dark brown residual oil was distilled at 0.5 m.m. (block temperature 140 - 145°)[16] to give 2-methyl-1-phenylindolizine (6.27 g, 20%) as a yellow-orange oil.

CI$_{12}$ 5-Methyl-2-phenylindolizine.

β-Bromopropiophenone was prepared essentially by the method used for the preparation of phenacyl bromide (Org. Synth. Vol. 19, p.24)

Bromine (16.1 mls, 0.315 mole) was added dropwise to a stirred solution of propiophenone (42 g, 0.315 mole) and aluminium chloride (0.5 g) in dry ether (45 mls). The colour of the bromine disappeared rapidly, and when all the bromine had been added the ethereal solution of β-bromopropiophenone was washed with water and dried (K_2CO_3). Evaporation of the solvent and subsequent distillation gave β-bromopropiophenone b.p. 134 - 136°/18 mm.

β-Bromopropiophenone (7.5 mls, 0.05 mole) wasadded to 2-picoline (5.65 mls, 0.05 mole) and the resulting solution was heated at 120° for ½ hour. The brown oil which had formed was titurated with acetone, and the white solid (6.75 g, 60%) which crystallised, was collected, washed with acetone, and crystallised from ethanol to give 1-1'-benzoylethyl-2-methylpyridinium bromide as colourless needles, m.p. 220 - 225° turning green > 210°.

Found N = 4.32 $C_{15}H_{16}BrNO$ requires N = 4.57

A solution of 1-1'-benzoylethyl-2-methylpyridinium bromide (3.06 g, 0.01 mole) and sodium hydrogen carbonate (5.0 g) in water (100 mls) was refluxed for 30 minutes, during which time a waxy precipitate of 5-methyl-2-phenylindolizine (1.393 g, 67%) formed.

The crude product recrystallised from ethanol as colourless waxy needles (1.096 g, 53%), m.p. 93 - 95°.

Found C = 86.45 H = 6.41 N = 7.21

$C_{15}H_{13}N$ requires C = 86.92 H = 6.33 N = 6.77

CI_{13} 5-Methyl-2-phenylindolizine was prepared by the method of Boekelheide and Windgassen.[20] 2,6-Dimethyl-1-phenacylpyridinium bromide, m.p. 220°(d), was obtained in 59% yield (lit. yield 62%; m.p. 220°(d)). This salt gave 5-methyl-2-phenylindolizine (89%), m.p. 80.5 - 81.5°, (lit. yield 86%; m.p. 81 - 81.5°).

CI_{14} 1,3-Dimethyl-2-phenylindolizine

A solution of 2-ethylpyridine (5.3 g, 0.05 mole) and β-bromopropiophenone (10.6 g, 0.05 mole) in chloroform (5 mls) was gently warmed until the solution became cloudy. On cooling and trituration with a little acetone 1-1'-benzoylethyl-2-ethylpyridinium bromide (4.2 g, 26%) precipitated as white crystals.

The mother liquors were poured into water and the mixture was extracted with ether. The quaternary salt which had precipitated was added to the aqueous layer followed by sodium hydrogen carbonate (10 g), and the resulting mixture was refluxed for 1 hour. Light brown crystals of the product separated from the solution. The crude product was sublimed at 13 mm (block temperature 130°) to give pure 1,3-dimethyl-2-phenylindolizine (3.25 g, 39%) as straw-coloured needles. m.p. 78.5 - 80.5°. Found C = 86.84 H = 6.93 N = 6.20

$C_{16}H_{15}N$ requires C = 86.83 H = 6.83 N = 6.33

CI_{15} Benzo [e] indolizine, was prepared by the method of Roberts, Gates and Boekelheide.[143] 1-(2-quinolyl)-2,3-propanediol, m.p. 114 - 115.5°, was obtained in 45% yield, (lit. yield 58%; m.p. 115 - 116°). This salt gave benzo (e) indolizine (83%), m.p. 108 - 108.5°, (lit. yield 85%; m.p. 108 - 108.5°).

CI_{16} 2,2'-Dimethylmethylene-3,3'-di-indolizine, was prepared by the method of Holland and Naylor.[111] 2-Methylindolizine (13.1 g, 0.1 mole) and 40% aqueous formaldehyde (6.5 mls) gave 2,2'-dimethylmethylene-3,3'-di-indolizine (1.16 g, 85%). A specimen sublimed at 10 mm (block temperature 170°) had m.p. 158 - 160.5°, (lit. yield 95%; m.p. 159 - 160°).

CI_{17} 1,2,2'-Trimethylmethylene-3,3'-di-indolizine.

To a suspension of sodium borohydride (2g) in methanol (25 mls) was added slowly with stirring a suspension of 3-(2-methylindolizin-3-yl) methylene-1,2-dimethylindolizinium perchlorate (3.87 g, 0.01 mole) in methanol (50 mls). The intense blue colour of the monomethine dye was discharged, with a supplementary addition of sodium borohydride (2 g), to give a pale yellow solution which on cooling deposited 1,2,2'-trimethylmethylene-3,3'-di-indolizine (1.96 g, 68%). These were collected, washed with a little methanol, and recrystallised from methanol as colourless needles, m.p. 125 - 129° (d).

Found C = 83.30 H = 6.99

$C_{20}H_{20}N_2$ requires C = 83.42 H = 7.11

CI_{18} 1,1'2,2'-Tetramethylmethylene-3,3'-di-indolizine

To a solution of 1,2-dimethylindolizine (5.80 g, 0.04 mole) in ethanol (30 mls) was added 40% aqueous formaldehyde (3 mls). Almost immediately an exothermic reaction occurred with the precipitation of clear prismatic needles of 1,1'2,2'-tetramethylmethylene-3,3'-di-indolizine (5.53 g, 92%). These were collected, washed with ethanol, and after recrystallisation from acetonitrile had m.p. 165 - 168°.

Found N = 9.62 $C_{21}H_{22}N_2$ requires N = 9.26

CI_{19} 2,2',3,3'-Tetramethylmethylene-1,1'-di-indolizine.

Addition of 40% aqueous formaldehyde (6.3 mls) to a solution of 2,3-dimethylindolizine (12.855 g) in ethanol (40 mls) gave a solution which became progressively deeper green and from which cream-yellow needles of 2,2'3,3'-tetramethylmethylene-1,1'-di-indolizine (7.118 g, 63%) slowly deposited on standing. These were collected, and after successive recrystallisation from ethanol andacetonitrile formed cream yellow needles, m.p. 109 - 110° (lit.[112] m.p. 109 - 110°).

Found C = 83.17   H = 7.07   N = 8.91

$C_{21}H_{22}N_2$ requires C = 83.4   H = 7.33   N = 9.26

CI_{20} 2,2'-Dimethyl-1,1'-diphenylmethylene-3,3'-di-indolizine.

To a solution of 2-methyl-1-phenylindolizine (4.14 g, 0.02 mole) in ethanol (15 mls) was added 40% aqueous formaldehyde (2.5 mls). Almost immediately cream-yellow needles of 2,2'-dimethyl-1,1'-diphenylmethylene-3,3'-di-indolizine (3.75 g, 88%) deposited. These were collected, washed with ethanol, dried in vacuo, and on being recrystallised from acetonitrile gave cream-yellow needles, m.p. 216.5 - 219.5° (d).

Found N = 6.48 $C_{31}H_{26}N_2$ requires N = 6.57

CII <u>Indolisinium Perchlorates.</u>

<u>General Procedure.</u>

To a solution of the indolizine (0.01 mols) in ethanol (10 mls) was added perchloric acid (1.2 mls, 25% excess). The indolizinium perchlorate deposited and was filtered off from the cooled solution. A further quantity was obtained by the addition of ether (50 mls) to the mother liquors. The product was washed with a small quantity of ethanol followed by ether, and unless otherwise stated recrystallised from ethanol containing 1% ($^{v}/_{v}$) perchloric acid.

CII_1 <u>Indolizinium perchlorate</u> was obtained as colourless needles (92%) which darkened in air, using methanol (20 mls) as solvent. In a deviation from the general procedure the addition of, and washing with, ether was omitted. Recrystallisation from methanol containing 1% ($^{v}/_{v}$) perchloric acid gave colourless needles, m.p. 181.5 - 186.5 (d).

Found N = 5.84 $C_8H_8ClNO_4$ requires N = 6.44

CII_2 <u>2-Methylindolizinium perchlorate</u> was obtained as colourless needles (96%), m.p. 92.5 - 94.5° (lit.[8] m.p. 92 - 93.5°).

CII_3 <u>1,2-Dimethylindolizinium perchlorate</u> was obtained as colourless needles (95%), m.p. 131-133° (lit.[112] m.p. 128 - 129°).

CII_4 <u>2,3-Dimethylindolizinium perchlorate</u> was obtained as colourless needles (97%) using methanol (20 mls) as solvent and was recrystallised from methanol containing 1% ($^{v}/_{v}$) perchloric acid, m.p. 60 - 67.5° when prepared from 2,3-dimethylindolizine obtained via CI_4(a), m.p. 61.5-67.5°

when prepared from 2,3-dimethylindolizine obtained via CI_4(b). (lit.[112] m.p. 74 - 75.5°).

CII_5 <u>2,6-Dimethylindolizinium perchlorate</u>, was obtained as colourless needles (88%), m.p. 145°.

Found N = 5.72 $C_{10}H_{12}ClNO_4$ requires N = 5.70

CII_6 <u>2,8-Dimethylindolizinium perchlorate</u>, was obtained as colourless needles (96%), m.p. 166 - 168°.

Found N = 5.80 $C_{10}H_{12}ClNO_4$ requires N = 5.70

CII_7 <u>3-Ethyl-2-methylindolizinium perchlorate</u>, was obtained as colourless needles (97%), m.p. 106 - 108°.

Found N = 5.07 $C_{11}H_{14}ClNO_4$ requires N = 5.39

CII_8 <u>1,2,3-Trimethylindolizinium perchlorate</u>, was obtained as colourless needles (98%), m.p. 126.5 - 129° when prepared from 1,2,3-trimethylindolizine obtained via CI_8 (a); m.p. 127 - 130.5° when prepared from 1,2,3-trimethylindolizine obtained via CI_8(b), (lit.[112] m.p. 126 - 128°).

CII_9 <u>2-Phenylindolizinium perchlorate</u> was obtained in (95%) yield using acetonitrile (50 mls) as solvent, and with the addition of ether to precipitate the product. Recrystallization from acetonitrile containing 1% (v/v) perchloric acid with the subsequent addition of ether gave colourless needles, m.p. 161.5 - 164°.

Found N = 4.95 $C_{14}H_{12}ClNO_4$ requires N = 4.77

CII$_{10}$ 1-Methyl-2-phenylindolizinium perchlorate was obtained as colourless needles (92%), m.p. 120 - 123.5°(d).

Found N = 4.37 $C_{15}H_{14}ClNO_4$ requires N = 4.55

CII$_{11}$ 2-Methyl-1-phenylindolizinium perchlorate was obtained as colourless needles (92%), m.p. 164 - 167° (lit.[119] m.p. 167 - 168.5°).

Found N = 4.54 $C_{15}H_{14}ClNO_4$ requires N = 4.55

CII$_{12}$ 3-Methyl-2-phenylindolizinium perchlorate was obtained as colourless needles (96%), m.p. 141 - 143.5°.

Found N = 4.54 $C_{15}H_{14}ClNO_4$ requires N = 4.55

CII$_{13}$ 5-Methyl-2-phenylindolizinium perchlorate was obtained as colourless needles (97.5%) using ethanol (30 mls) as solvent and had mp. 231 - 235°(d).

Found N = 4.47 $C_{15}H_{14}ClNO_4$ requires N = 4.55

CII$_{14}$ 1,3-Dimethyl-2-phenylindolizinium perchlorate was obtained as colourless plates (97.5%), recrystallised from methanol containing 1% ($^v/_v$) perchloric acid as colourless needles, m.p. 114.5 - 116°.

Found N = 4.35 $C_{16}H_{16}ClNO_4$ requires 4.35

CII$_{15}$ Benzo (e) indolizinium perchlorate was obtained as colourless needles (78%) which acquired a faint violet colour in air, using acetonitrile (40 mls) as solvent and was recrystallised from acetonitrile containing 1% ($^v/_v$) perchloric acid, m.p. 167 - 169°.

Found N = 4.95 $C_{12}H_{10}ClNO_4$ N = 5.23

CIII <u>Ethoxymethyleneindolizinium Salts.</u>

CIII(a) <u>Stable Ethoxymethyleneindolizinium salts.</u>

<u>General Procedure.</u>

Ethyl orthoformate (15 mls, 0.09 mole) was added to a solution of the indolizinium perchlorate (0.01 mole) in ethanol (15 mls). Almost immediately the solution became blue-green and green or yellow crystals deposited. After the solution had been cooled for 10 minutes the ethoxymethyleneindolizinium perchlorate was filtered off, washed with ethanol, followed by ether, and dried in vacuo. In the case of the more stable ethoxymethyleneindolizinium perchlorates a specimen was recrystallised from methanol for analysis.

CIII $(a)_1$ <u>3-Ethoxymethylene-2-methylindolizinium perchlorate</u> was obtained as green needles (92%), m.p. 216 - 217.5°.

Found N = 4.80 $C_{12}H_{14}ClNO_5$ requires N = 4.87

CIII $(a)_2$ <u>3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate</u> was obtained as yellow needles (70%), and recrystallised unchanged in form from methanol, m.p. 210 - 218°

Found C = 51.65 H = 5.34 N = 4.40 Cl = 11.81

$C_{13}H_{16}ClNO_5$ requires C = 51.80 H = 5.30 N = 4.60 Cl = 11.75

CIII $(a)_3$ <u>3-Ethoxymethylene-1,2-dimethylindolizinium Iodide.</u>

A solution of anhydrous sodium iodide (12 g, 0.08 mole) in acetone (60 ml) at the boiling point was added to one of 3-ethoxymethylene-1,2-dimethylindolisinium perchlorate (6.04 g 0.02 mole) in acetonitrile (40 ml, saturated solution) at the boiling point. The product began to crystallise from the boiling solution. Filtration of the cooled solution gave orange-yellow plates (or yellow needles) (4.69g, 71%) which were washed with a small volume of acetone followed by acetone-ether (1:2), then ether. They were dried for 10 minutes at 100° for analysis; and had m.p. 136-137° (decomp. to green liquid).

Found N = 4.06 $C_{13}H_{16}INO$ requires N = 4.3

CIII (a)$_4$ <u>1-Ethoxymethylene-2,3-dimethylindolisinium perchlorate</u> was obtained as yellow needles (96%) and recrystallised from methanol, m.p. 240° (preheated block).

Found N = 4.68 $C_{13}H_{16}ClNO_5$ requires N = 4.64

CIII (a)$_5$ <u>3-Ethoxymethylene-2,6-dimethylindolisinium perchlorate</u> was obtained as light green needles (30%) m.p. 142 - 167°

Found N = 4.67 $C_{13}H_{16}ClNO_5$ requires N = 4.64

CIII (a)$_6$ <u>3-Ethoxymethylene-2,8-dimethylindolisinium perchlorate</u> was obtained as green needles (68%), m.p. 196.5-199°.

Found N = 4.41 $C_{13}H_{16}ClNO_5$ requires N = 4.64

CIII (a)$_7$ <u>1-Ethoxymethylene-3-ethyl-2-methylindolisinium perchlorate</u> was obtained as green-yellow needles (46%) which were recrystallised from methanol, m.p. 167.5 - 168.5°.

Found N = 4.26 $C_{14}H_{18}ClNO_5$ requires N = 4.44

CIII (a)$_8$ <u>3-Ethoxymethylene-1-methyl-2-phenylindolisinium perchlorate</u> was obtained as yellow-green microcrystals(83%), and was recrystallised from methanol, m.p. 138 - 146°.

Found N = 4.05 $C_{18}H_{18}ClNO_5$ requires N = 3.87

CIII (a)$_9$ <u>3-Ethoxymethylene-2-methyl-1-phenylindolizinium perchlorate</u> was obtained as green needles (86%) using warm ethanol (20 mls), as solvent. It was recrystallised from methanol, m.p. 152 - 180°.

Found N = 4.28 $C_{18}H_{18}ClNO_5$ requires N = 3.87

CIII (a)$_{10}$ <u>1-Ethoxymethylene-3-methyl-2-phenylindolizinium perchlorate</u> was obtained as light green needles (67%) using warm ethanol (250 mls), and was recrystallised from methanol, m.p. 194 - 196°.

Found N = 4.29 $C_{18}H_{18}ClNO_5$ requires N = 3.87

CIII (a)$_{11}$ <u>3 (or 1)-Ethoxymethylene-5-methyl-2-phenylindolizinium perchlorate</u> was obtained as yellow needles (86%) using warm acetic anhydride (20 mls) as solvent and was recrystallised from methanol, m.p. 186 - 188.5° (d).

Found N = 4.53 $C_{18}H_{18}ClNO_5$ requires N = 3.87

CIII (b) <u>Transient Ethoxymethyleneindolizinium perchlorates.</u>

CIII (b)$_1$ <u>Reaction of indolizinium perchlorate with ethyl orthoformate</u>

To a solution of indolizinium perchlorate (0.217 g, 0.001 mole) in ethanol (10 mls) was added ethyl orthoformate (1.5 mls, 0.09 mole). The solution turned crimson-red, then violet and deposited small black needles of <u>3-(indolizin-3-yl)methylene indolizinium perchlorate</u> (0.139 g, 40.5%). These were collected from the cooled solution washed with a small volume of ethanol followed by ether and recrystallised from acetonitrile - methanol (5:1). It had m.p. > 240° (pre-heated block), λ max. 573.

Found N = 7.85 $C_{17}H_{15}ClN_2O_4$ requires N = 8.13

CIII (b)$_2$ Reaction of 2-phenylindolizinium perchlorate with ethyl orthoformate

To a solution of 2-phenylindolizinium perchlorate (2.94 g, 0.01 mole) in ethanol (25 mls) was added ethyl orthoformate (15 mls, 0.09 mole). The resulting dark green solution on scratching and thorough cooling did not afford any precipitate; and the addition of ether produced a small quantity of a blue oily precipitate.

The above procedure was repeated using acetonitrile (10 mls) as solvent in place of ethanol. The dark green solution on cooling and addition of ether precipitated yellow green crystals of 3-ethoxymethylene-2-phenylindolizinium perchlorate (2.75 g, 78%). These were collected and washed with a little ether. Within 10 minutes the exposed surfaces and finally the total mass of collected crystals became dark blue green.

CIII (b)$_3$ Reaction of benzo (e) indolizine with ethyl orthoformate in the presence of perchloric acid.

To a solution of benzo (e) indolizine (1.67 g, 0.01 mole) in ethanol (20 mls) was added ethyl orthoformate (15 mls, 0.09 mole) followed by perchloric acid (1.5 mls). This gave initially a dark green solution which eventually turned blue-violet and deposited black needles of 3-(benzo (g) indolizin-3-yl) methylene-benzo(g) indolizinium perchlorate (1.85 g, 41%). These were collected, washed with a small volume of ethanol, followed by ether, and recrystallised from acetonitrile. It did not melt < 340°, λ max. 561.

Found N = 5.97 $C_{25}H_{17}ClN_2O_4$ requires N = 6.30

CIII (c) Reaction of 1,3-Disubstituted Indolizinium Perchlorates with Ethyl Orthoformate.

CIII $(c)_1$ Reaction of 1,2,3-trimethylindolizinium perchlorate with ethyl orthoformate.

Ethyl orthoformate (15 mls, 0.09 mole) was added to a solution of 1,2,3-trimethylindolizinium perchlorate (2.59 g, 0.01 mole) in ethanol (15 mls). No colour change occurred even on prolonged refluxing and 1,2,3-trimethylindolizinium perchlorate (2.565 g, 99%), m.p. 128.5 - 130°, was recovered.

CIII $(c)_2$ Reaction of 1,3-dimethyl-2-phenylindolizinium perchlorate with ethyl orthoformate.

Ethyl orthoformate (15 mls, 0.09 mole) was added to a solution of 1,3,-dimethyl-2-phenylindolizinium perchlorate (3.20 g, 0.01 mole) in ethanol (15 mls). No colour change occurred even on prolonged refluxing and 1,3-dimethyl-2-phenylindolizinium perchlorate (3.15 g, 98%), m.p. 114.5 - 116°, was recovered.

CIV <u>Condensation of 3 (1)-Ethoxymethyleneindolizinium salts with Heterocyclic Quaternary Ammonium Salts in the presence of Piperidine</u>

<u>General Procedure.</u>

A solution of the 3(1)-ethoxymethyleneindolizinium salt (0.005 mole) and the heterocyclic quaternary ammonium salt (0.005 mole) in acetonitrile (10 mls with monocyclic; 20 mls with bicyclic heterocyclic quaternary ammonium salts) containing piperidine (0.5 ml, 100% excess) was refluxed for 4 minutes. The product was filtered from the cooled solution, washed successively with water to remove piperidinium perchlorate, with a small volume of ethanol and finally with ether. Unless otherwise stated the product was recrystallised from acetonitrile. Visible spectra were measured in methanol containing 2% ($^{v}/v$) perchloric acid.

CIV_1 <u>3-Ethoxymethylene-2-methylindolizinium perchlorate with 1,4-dimethylpyridinium perchlorate.</u>

<u>1-Methyl-4-[2-(2-methylindolizin-3-yl) vinyl] pyridinium perchlorate</u> (21.5%) was obtained as crimson-red needles, m.p. > 295° (d), λ max. 521 (4.73).

Found N = 8.13 $C_{17}H_{17}ClN_2O_4$ requires N = 8.03

CIV_2 3-Ethoxymethylene-2-methylindolizinium perchlorate with 2,3-dimethylthiazolium perchlorate.

3-Methyl-2-(2-(2-methylindolizin-3-yl) vinyl) thiazolium perchlorate (21.5%) was obtained as grey-red needles, m.p. > 252 - 255° (preheated block), λ max. 525 (broad) (4.68).

Found N = 8.16 $C_{15}H_{15}ClN_2O_4S$ requires N = 7.90

CIV_3 3-Ethoxymethylene-2-methylindolizinium perchlorate with 1,2-dimethylquinolinium perchlorate.

1-Methyl-2-(2-(2-Methylindolizin-3-yl)vinyl)quinolinium perchlorate (38%) was obtained as green needles, m.p. 300.5 - 301° (d), λ max. 565 (4.89).

Found N = 6.89 $C_{21}H_{19}ClN_2O_4$ requires N = 7.03

CIV_4 3-Ethoxymethylene-2-methylindolizinium perchlorate with 1,4-dimethylquinolinium perchlorate.

1-Methyl-4-(2-(2-methylindolizin-3-yl)vinyl)quinolinium perchlorate (35%) was obtained as dark green needles, m.p. 276 - 277.5°, λ max. 595 (4.78).

Found N = 7.09 $C_{21}H_{19}ClN_2O_4$ requires N = 7.03

CIV_5 3-Ethoxymethylene-2-methylindolizinium perchlorate with 2,3-dimethylbenzoxazolium perchlorate.

3-Methyl-2-(2-(2-methylindolizin-3-yl)vinyl)benzoxazolium perchlorate (16.5%) was obtained as red needles, m.p. 306.5 - 308.5°, λ max. 519 (4.92).

Found N = 7.32 $C_{19}H_{17}ClN_2O_5$ requires N = 7.21

CIV_6 <u>3-Ethoxymethylene-2-methylindolizinium perchlorate with 2,3-dimethylbenzothiazolium perchlorate</u>.

<u>3-Methyl-2-(2-(2-methylindolizin-3-yl)vinyl)benzothiazolium perchlorate</u> (87%) was obtained as brown green needles, m.p. 305 - 306°(d), λ max. 550 (4.91).

Found N = 7.15% $C_{19}H_{17}ClN_2O_4S$ requires N = 6.92

CIV_7 <u>3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with 1,2-dimethylpyridinium perchlorate</u>.

<u>1-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl)pyridinium perchlorate</u> (19%) was obtained as red needles, m.p. 237°(d), λ max. 531 (4.66).

Found N = 7.65 $C_{18}H_{19}ClN_2O_4$ requires N = 7.73

CIV_8 <u>3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with 1,2-dimethylpyridinium iodide.</u>

<u>1-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl)pyridinium iodide</u> (17%) was obtained as black needles, m.p. > 350°, λ max. 551 (4.65).

Found N = 6.85   I = 31.91

$C_{18}H_{19}IN_2$ requires N = 7.18   I = 32.51

CIV$_9$ <u>3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with 1,4-dimethylpyridinium perchlorate.</u>

<u>1-methyl-4-(2-(1,2-dimethylindolizin-3-yl)vinyl)pyridinium perchlorate</u> (12%) was obtained as red-brown needles, m.p. 290 - 291° (d), λ max. 536 (4.70).

Found C = 59.66 H = 5.37

$C_{18}H_{19}ClN_2O_4$ requires C = 59.59 H = 5.28

CIV$_{10}$ <u>3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with 2,3-dimethylthiazolium perchlorate.</u>

<u>3-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl)thiazolium perchlorate</u> (67%) was obtained as violet-needles, m.p. 258.5 - 260°, λ max. 542 (4.70).

Found N = 7.55 S = 8.45

$C_{16}H_{17}ClN_2O_4S$ requires N = 7.59 S = 8.69

CIV$_{11}$ <u>3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with 2,3,4-trimethylthiazolium perchlorate.</u>

<u>3,4-Dimethyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl)thiazolium perchlorate</u> (36.8%) was obtained as violet-black needles, m.p. 296° with slow dec > 335°, λ max. 544 (4.67).

Found N = 7.45 S = 8.40 Cl = 9.25

$C_{17}H_{19}ClN_2O_4S$ requires N = 7.31 S = 8.36 Cl = 9.25

CIV_{12} *3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with 1,2-dimethylquinolinium perchlorate.*

1-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl)quinolinium perchlorate (68.5%) was obtained as green needles, slow dec. > 325°, λ max. 573 (4.88).

Found C = 65.76 H = 5.11 N = 6.89

$C_{22}H_{21}ClN_2O_4$ requires C = 64.00 H = 5.13 N = 6.78

CIV_{13} *3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with 1,4-dimethylquinolinium iodide.*

1-Methyl-4-(2-(1,2-dimethylindolizin-3-yl)vinyl)quinolinium iodide (81%) was obtained as greenish yellow needles, m.p. 286°, λ max. 621 (4.78).

Found N = 5.88 $C_{22}H_{21}IN_2$ requires N = 6.37

CIV_{14} *3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with 2,3-dimethylbenzoxazolium perchlorate.*

3-Methyl-2-(2-(1,2-dimethylindolizin-3-yl)vinyl)benzoxazolium perchlorate (37%) was obtained as crimson needles, m.p. > 325° (preheated block) λ max. 534 (4.93).

Found C = 59.87 H = 4.74 N = 6.51 Cl = 8.67

$C_{20}H_{19}ClN_2O_5$ requires C = 59.63 H = 4.75 N = 6.96 Cl = 8.80

CIV_{15} 3-Ethoxymethylene-1.2-dimethylindolizinium perchlorate with 2.3-dimethylbenzothiazolium perchlorate.

3-Methyl-2-(2-(1.2-dimethylindolizin-3-yl)vinyl)benzothiazolium perchlorate (89%) was obtained as green needles, m.p. 308.5 - 309°, λ max. 571 (4.96).

Found Cl = 8.73 N = 6.86 S = 7.96

$C_{20}H_{19}ClN_2O_4S$ requires Cl = 8.46 N = 6.69 S = 7.66

CIV_{16} 3-Ethoxymethylene-2.6-dimethylindolizinium perchlorate with 2.3-dimethylthiazolium perchlorate.

3-Methyl-2-(2-(2.6-dimethylindolizin-3-yl)vinyl)thiazolium perchlorate (78%) was obtained as red needles, m.p. 298°, λ max. 535 (4.68).

Found N = 7.93 $C_{16}H_{17}ClN_2O_4S$ requires N = 7.60

CIV_{17} 3-Ethoxymethylene-2.6-dimethylindolizinium perchlorate with 1.4-dimethylquinolinium perchlorate.

1-Methyl-4-(2-(2.6-dimethylindolizin-3-yl)vinyl)quinolinium perchlorate (87%) was obtained as green needles, m.p. > 315° (preheated block), λ max. 609 (4.81).

Found N = 7.23 $C_{22}H_{21}ClN_2O_4$ requires N = 6.79

CIV_{18} 3-Ethoxymethylene-2.6-dimethylindolizinium perchlorate with 2.3-dimethylbenzoxazolium perchlorate.

3-Methyl-2-(2-(2.6-dimethylindolizin-3-yl)vinyl)benzoxazolium perchlorate (61%) was obtained as crimson red needles, m.p. > 317° (preheated block), λ max. 527 (4.97).

Found N = 7.10 $C_{20}H_{19}ClN_2O_5$ requires N = 6.95

CIV_{19} <u>3-Ethoxymethylene-2,6-dimethylindolizinium perchlorate with 2,3-dimethylbenzothiazolium perchlorate.</u>

<u>3-Methyl-2-(2-(2,6-dimethylindolizin-3-yl)vinyl)benzothiazolium perchlorate</u> (88%) was obtained as dark brown needles, m.p. 310 - 311° (d), λ max. 561 (4.96).

Found N = 6.73 $C_{20}H_{19}ClN_2O_4S$ requires N = 6.69

CIV_{20} <u>3-Ethoxymethylene-2,8-dimethylindolizinium perchlorate with 2,3-dimethylbenzothiazolium perchlorate.</u>

<u>3-Methyl-2-(2,8-dimethylindolizin-3-yl)vinyl)benzothiazolium perchlorate</u> 52% was obtained as crimson needles, m.p. > 305° (preheated block), λ max. 567 (4.98).

Found N = 6.76 $C_{20}H_{19}ClN_2O_4S$ requires N = 6.69

CIV_{21} <u>3-Ethoxymethylene-1-methyl-2-phenylindolizinium perchlorate with 2,3-dimethylbenzoxazolium perchlorate.</u>

<u>3-Methyl-2-(2-(1-methyl-2-phenylindolizin-3-yl)vinyl)benzoxazolium perchlorate</u> (87%) was obtained as golden green needles, m.p. 257.5 - 260°, λ max. 536 (4.90).

Found N = 6.06 $C_{25}H_{21}ClN_2O_5$ requires N = 6.05

CIV$_{22}$ <u>3-Ethoxymethylene-1-methyl-2-phenylindolizinium perchlorate with 2,3-dimethylbenzothiazolium perchlorate</u>.

<u>3-Methyl-2-(2-(1-methyl-2-phenylindolizin-3-yl)vinyl)benzothiazolium perchlorate</u> (46%) was obtained as golden needles, m.p.285.5 - 289°, λ max. 373 (4.95).

Found N = 6.24 $C_{25}H_{21}ClN_2O_4S$ requires N = 5.85

CIV$_{25}$ <u>1-Ethoxymethylene-3-methyl-2 phenylindolizinium perchlorate with 2,3-dimethylbenzoxazolium perchlorate.</u>

<u>3-Methyl-2-(2-(3-methyl-2-phenylindolizin-1-yl)vinyl)benzoxazolium perchlorate</u> (24%) was obtained as red needles, m.p. 300 - 301°, λ max. 508 (4.96).

Found N = 5.76 $C_{15}H_{21}ClN_2O_5$ requires N = 6.03

Condensation of Transient 3-Ethoxymethyleneindolizinium Perchlorates with Heterocyclic Quaternary Ammonium Salts.

CIV$_{24}$ 3-Ethoxymethyleneindolizinium perchlorate with 2,3-dimethylbenzothiazolium perchlorate.

To a solution of indolizinium perchlorate (0.654g, 0.003 mole) in acetonitrile-ethanol (1:5, 10 mls) was added ethyl orthoformate (4.5 mls, 0.0273 mole), immediately followed by piperidine (0.3 mls, 100% excess) and 2,3-dimethylbenzothiazolium perchlorate (0.788 g, 0.003 mole). The resulting mixture was refluxed for 4 minutes to give a crimson solution from which small dark crimson needles of 3-Methyl-2-(2-(indolizin-3-yl)vinyl)benzothiazolium perchlorate (0.336 g, 29%) deposited on cooling. These were collected, washed with a small volume of ethanol, then ether. Recrystallisation from acetonitrile-ethanol (1:5) gave small crimson needles, m.p. 244 - 247°, λ max. 387 (4.70).

Found N = 7.51 $C_{18}H_{15}ClN_2O_4S$ requires N = 7.17

CIV$_{25}$ 3-Ethoxymethylene-2-phenylindolizinium perchlorate with 2,3-dimethylbenzothiazolium perchlorate.

To a solution of 2-phenylindolizinium perchlorate (0.882 g, 0.003 mole) in acetonitrile-ethanol (1:5, 20 mls) was added ethyl orthoformate (4.5 mls, 0.0273 mole), followed by piperidine (0.3 mls, 100% excess) and 2,3-dimethylbenzothiazolium perchlorate (0.788 g, 0.003 mole). The resulting mixture was refluxed for 4 minutes to give a crimson-red solution from which golden-brown plates of 3-Methyl-2(2-(2-phenyl-

<u>indolizin-3-yl)vinyl)benzothiazolium perchlorate</u> (0.54g, 38.5%) deposited on cooling. These were collected, washed with a little ethanol, followed by ether, and on recrystallisation from acetonitrile-ethanol (1:5) gave golden-brown plates, m.p. 220-223°, λ max. 536 (4.73).

Found N = 5.90 $C_{24}H_{19}ClN_2O_4S$ requires N = 5.90

CIV$_{26}$ <u>3-Ethoxymethylene benzo (e) indolizinium perchlorate with 2,3-dimethylbenzothiazolium perchlorate.</u>

To a solution of benzo (e) indolizine (0.501g, 0.003 mole) in acetonitrile (10 mls) was added perchloric acid (60% ($^w/_w$), 0.50 mls) and ethyl orthoformate (4.6 mls, 0.0275 mole). Piperidine (0.3 ml, 100% excess) and 2,3-dimethylbenzothiazolium perchlorate (0.786g, 0.003 mole) were added immediately and the resulting mixture was refluxed for 4 minutes. The crimson solution deposited greenish-brown needles of <u>3-Methyl-2-(2-(benzo(e)indolizin-3-yl)vinyl)benzothiazolium perchlorate</u> (0.71g, 54%), which were collected, washed with a little ethanol, then with ether, and recrystallised from acetonitrile. It had m.p. > 340° with slow dec. > 300°, λ max. 561 (5.16).

Found N = 6.05 $C_{22}H_{17}N_2O_4S$ requires N = 6.35

CV Monomethine Dyes from Indolizine.

CV (a) Condensation of 3-Ethoxymethyleneindolizinium Perchlorate with Indolizines.

General Procedure.

To a solution of the indolizine (0.002 mole) in methanol or ethanol (12.5 mls) was added the 3-ethoxymethyleneindolizinium perchlorate (0.002 mole), and the resulting mixture was refluxed for 4 minutes. The resulting intensely blue (violet) solution deposited the 3-(indolizin-3-yl)methylene indolizinium perchlorate. After the solution had been cooled the product was collected, washed with a little ethanol, followed by ether, dried and recrystallised. Visible spectra were measured in methanol containing 2% ($^v/_v$) perchloric acid.

CV $(a)_1$ 2-Methylindolizine with 3-ethoxymethylene-2-methylindolizinium perchlorate.

3-(2-Methylindolizin-3-yl)methylene-2-methylindolizinium perchlorate prepared in methanol, recrystallised from acetonitrile-ethanol (1:4) as violet-black clusters of needles with a green reflex (73%), m.p. 225 - 226° (softens > 222°), λ max. 582 (4.65).

Found C = 61.55 H = 4.97

$C_{19}H_{17}ClN_2O_4$ requires C = 61.2 H = 4.6

CV $(a)_2$ 2-Methylindolizine with 3-ethoxymethylene-1,2-dimethylindolizinium perchlorate.

3-(2-Methylindolizin-3-yl)methylene-1,2-dimethylindolizinium perchlorate prepared in methanol, recrystallised from methanol as green prisms with a golden reflex (87%), m.p. 231 - 235.5° (preheated block to 210°), λ max. 595 (4.64)

Found C = 61.96 H = 5.08 N = 7.55

$C_{20}H_{19}ClN_2O_4$ requires C = 62.1 H = 4.95 N = 7.24

CV $(a)_3$ <u>2-Methylindolisine with 3-ethoxymethylene-2,6-dimethyl-indolisinium perchlorate</u>

<u>3-(2-Methylindolisin-3-yl)methylene-2,6-dimethylindolisinium</u> perchlorate (96%) was obtained as a dark blue non-crystalline mass from ethanol, and was recrystallised from ethanol by slow cooling and evaporation in a vacuum dessicator containing concentrated sulphuric acid. It had m.p. 201 - 208°, λ max. 597 (4.64).

Found N = 7.32 $C_{20}H_{19}ClN_2O_4$ requires N = 7.24

CV $(a)_4$ <u>2-Methylindolisine with 3-ethoxymethylene-2,8-dimethyl-indolisinium perchlorate.</u>

<u>3-(2-Methylindolisin-3-yl)methylene-2,8-dimethylindolisinium perchlorate</u> (82%) was obtained as a dark blue non-crystalline mass from ethanol and was recrystallised from ethanol by slow cooling and evaporation in a vacuum dessicator containing concentrated sulphuric acid. It had m.p. 227 - 230°, λ max. 591 (4.57).

Found N = 6.99 $C_{20}H_{19}ClN_2O_4$ requires N = 7.24

CV $(a)_5$ 2-Methylindolizine with 3-ethoxymethylene-1-methyl-2-phenylindolizinium perchlorate.

3-(2-Methylindolizin-3-yl)methylene-1-methyl-2-phenylindolizinium perchlorate (46%) was prepared in methanol, and was recrystallised from methanol, blue needles, m.p. 200-207°, λ max. 620 (4.52).

Found N = 6.33 $C_{25}H_{21}ClN_2O_4$ requires N = 6.24

CV $(a)_6$ 1,2-Dimethylindolizine with 3-ethoxymethylene-1,2-dimethylindolizinium perchlorate

3-(1,2-Dimethylindolizin-3-yl)methylene-1,2-dimethylindolizinium perchlorate (88%) was prepared in methanol. It was recrystallised from methanol, golden-green plates, m.p. > 261° with dec. λ max. 630 (4.62). (lit.[124] λ max. 628).

Found N = 6.82 $C_{21}H_{21}ClN_2O_4$ requires N = 6.99

CV $(a)_7$ 1-Methyl-2-phenylindolizine with 3-ethoxymethylene-1,2-dimethylindolizinium perchlorate.

3-(1,2-Dimethylindolizin-3-yl)methylene-1-methyl-2-phenylindolizinium perchlorate (82%) prepared in methanol, recrystallised from methanol as brown-gold needles, m.p. 250.5 - 252°, λ max. 636 (4.63).

Found N = 5.85 $C_{26}H_{23}ClN_2O_4$ requires N = 6.06

CV (a)$_8$ 1-Methyl-2-phenylindolizine with 3-ethoxymethylene-2,6-dimethylindolizinium perchlorate.

3-(2,6-Dimethylindolizin-3-yl)methylene-1-methyl-2-phenyl-indolizinium perchlorate (35.5%) was prepared in ethanol. It was recrystallised from methanol as small blue needles, m.p. > 235° (preheated block), λ max. 652 (4.31).

Found N = 6.54 $C_{26}H_{23}ClN_2O_4$ requires N = 6.07

CV (a)$_9$ 1-Methyl-2-phenylindolizine with 3-Ethoxymethylene-2,8-dimethylindolizinium perchlorate.

3-(2,8-Dimethylindolizin-3-yl)methylene-1-methyl-2-phenyl-indolizinium perchlorate (86%) was prepared in methanol. It recrystallised from methanol as a blue amorphous solid, m.p. 70 -100°, λ max. 628 (4.30).

Found N = 6.01 $C_{26}H_{23}ClN_2O_4$ requires N = 6.07

CV (b) Condensation of Indolizine Aldehydes with Indolizinium Perchlorates.

CV (b)$_1$ 3-Formyl-2-methylindolizine with 2-methylindolizinium perchlorate.

To a solution of 3-formyl-2-methylindolizine (0.795g, 0.005 mole) in methanol (20 mls) was added 2-methylindolizinium perchlorate (1.15 g, 0.005 mole). The resulting mixture, refluxed for 4 minutes, gave an intense blue colouration and deposited 3-(2-Methylindolizin-3-yl) methylene-2-methylindolizinium perchlorate (1.001g, 58%). Recrystallisation from acetonitrile-ethanol (1:4) gave violet-black clusters of needles with a green reflex, m.p. 224 - 226° (softens > 222°), λ max. 583.

CV (b)$_2$ 1-Formyl-2,3-dimethylindolizine with 2,3-dimethylindolizinium perchlorate.

To a solution of 1-formyl-2,3-dimethylindolizine (0.346 g, 0.002 mole) in methanol (10 mls) was added 2,3-dimethyl-indolizinium perchlorate (0.490 g, 0.002 mole), and the resulting mixture was refluxed for 4 minutes. An intense violet colour developed and deposition of 1-(2,3-dimethylindolizin-1-yl)methylene-2,3-dimethyl-indolizinium perchlorate (0.727 g, 97%) occurred. Recrystallisation from methanol gave golden-green needles, m.p. 265 - 268.5° (d), λ max. 586 (lit.[124] m.p. 270 - 273°(d), λ max 587).

CV (c) Condensation of Azulene Aldehydes with Indolizinium Perchlorates General Procedure.

The azulene aldehyde (0.001 or 0.0015 mole) and the indolizinium perchlorate (0.001 or 0.0015 mole) in methanol (10 mls) were refluxed for 2 minutes. The product which deposited from the cooled solution was collected and recrystallised. Visible spectra were measured in methanol containing 1% (v/v) perchloric acid.

CV (c)$_1$ 1-Formylazulene with 2-methylindolizinium perchlorate.

3-(Azulene-1-yl)methylene-2-methylindolizinium perchlorate (100%)

recrystallised from acetonitrile as black needles, m.p. 260 - 261.5°(d) λ max. 575 (4.65)

Found N = 3.2 $C_{20}H_{16}ClNO_4$ requires N = 3.8

CV (c)$_2$ <u>1-Formylazulene with 1,2-dimethylindolizinium perchlorate</u>

3-(Azulen-1-yl)methylene-1,2-dimethylindolizinium perchlorate (93%), recrystallised from acetonitrile as black needles with a green reflex, m.p. 253 - 255.5°(d), λ max. 568 (4.58). (lit.[125] λ max. 580).

Found N = 3.5 $C_{21}H_{18}ClNO_4$ requires N = 3.7

CV (c)$_3$ <u>1-Formylazulene with 2,6-dimethylindolizinium perchlorate</u>

<u>3-(Azulen-1-yl)methylene-2,6-dimethylindolizinium perchlorate</u> (97%), recrystallised from acetonitrile as black needles, m.p. 273 - 274°(d), λ max. 566 (4.64).

Found N = 3.6 $C_{21}H_{18}ClNO_4$ requires N = 3.7

CV (c)$_4$ <u>1-Formyl-3-methylazulene with 1,2-dimethylindolizinium perchlorate</u>.

3-(3-Methylazulen-1-yl)methylene-1,2-dimethylindolizinium perchlorate (86%), recrystallised from acetonitrile as brown crystals (indefinite form), m.p. 268 - 270°, λ max. 604 (4.62).

Found N = 3.51 $C_{22}H_{20}ClNO_4$ requires N = 3.52

CV (c)$_5$ <u>3-Formylguiazulene with 1,2-dimethylindolizinium perchlorate</u>

<u>3-(3,8-dimethyl-5-isopropylazulen-1-yl)methylene-12-dimethyl indolizinium perchlorate</u> (94%), recrystallised from methanol as dark

green needles, m.p. 211.5 - 213°, λ max. 648 (4.68)

Found N = 3.4 $C_{26}H_{25}ClNO_4$ requires N = 3.1

CV (d) <u>Condensation of Ethoxymethyleneindolizinium Perchlorates with Azulenes.</u>

CV $(d)_1$ <u>3-Ethoxymethylene-2-methylindolizinium perchlorate with 1-methylazulene.</u>

A mixture of 3-ethoxymethylene-2-methylindolizinium perchlorate (0.288 g, 0.001 mole) and 1-methylazulene (0.142 g, 0.001 mole) in ethanol (5 mls) was boiled for 5 minutes. The product crystallised at once from the boiling blue solution and was filtered from the cooled solution. Recrystallisation from acetonitrile-ethanol (1:2) (by dissolution in boiling acetonitrile, filtration, and evaporation of solvent until the product had just begun to crystallise, followed by addition of twice the volume of boiling ethanol) gave 3-(3-methylazulen-1-yl)methylene-2-methylindolizinium perchlorate (0.305 g, 80%) as green needles, m.p. 282 - 284°(d), (block preheated to 270°), λ max. (methanol containing 1% (V/V) perchloric acid) 608 (4.68).

Found C = 65.45 H = 4.86 N = 3.91

$C_{21}H_{18}ClNO_4$ requires C = 65.7 H = 4.7 N = 3.70

CV $(d)_2$ <u>3-Ethoxymethylene-2,6-dimethylindolizinium perchlorate with 1-methylazulene</u>

A solution of 3-ethoxymethylene-2,6-dimethylindolizinium perchlorate (0.302 g, 0.001 mole) and 1-methylazulene (0.142 g, 0.001 mole) in methanol (6.5 ml) gave after boiling for 2 minutes violet-black needles of the perchlorate (0.186 g, 47%). After recrystallisation from acetonitrile 3-(3-methylazulen-1-yl)methylene-2,6-dimethylindolizinium perchlorate was obtained as green needles m.p. 279.5 - 281° (d) λmax. (methanol containing 1% perchloric acid) 606 (4.66).

Found N = 3.05 $C_{22}H_{20}ClNO_4$ requires N = 3.52

CV (e) Condensation of Ethoxymethyleneindolizinium Salts with Indole.

CV $(e)_1$ 3-Ethoxymethylene-2-methylindolizinium iodide with indole

3-Ethoxymethylene-2-methylindolizinium iodide (0.630 g, 0.002 mole) and indole (0.234 g, 0.002 mole) in ethanol (12.5 mls) were boiled for 5 minutes. The red solution on cooling deposited 3-(indol-3-yl) methylene-2-methylindolizinium iodide (0.304 g, 39%) which was recrystallised from acetonitrile as small dark brown needles, m.p. 223 - 224° (d).

Found N = 8.7 $C_{18}H_{15}IN_2$ requires N = 7.3

CV $(e)_2$ 3-Ethoxymethylene-1,2-dimethylindolizinium iodide with indole.

3-Ethoxymethylene-1,2-dimethylindolizinium iodide (0.658 g, 0.002 mole) and indole (0.234 g, 0.002 mole) in ethanol (12.5 mls) were boiled for 5 minutes. The red solution on cooling deposited 3-(indol-3-yl)methylene-1,2-dimethylindolizinium iodide (0.365 g, 46%), which recrystallised from methanol as brown needles m.p. 248.5 - 257.5 (d).

Found N = 8.6 $C_{19}H_{17}IN_2$ requires 7.0

CVI Preparation of Indolizine Aldehydes.

Ethoxymethyleneazulenium salts are readily hydrolysed by water to the corresponding aldehydes.[122] In contrast preliminary experiments showed that ethoxymethyleneindolizinium perchlorates were resistant to both neutral and alkaline hydrolysis. Accordingly the following procedure was adopted for the conversion to aldehyde:

Reaction of the ethoxymethyleneindolizinium perchlorate with a secondary amine afforded a dialkyl (or alkyl-aryl) aminomethyleneindolizinium perchlorate. In a number of cases these aminomethyleneindolizinium salts were isolated. Alkaline hydrolysis of the dialkylaminomethyleneindolizinium perchlorate produced the corresponding indolizine aldehyde. A more expeditious procedure, in which the yield of indolizine aldehyde was improved, involved the direct addition of the alkali to a mixture of the ethoxymethyleneindolizinium perchlorate, excess amine and a small volume of methanol, without the isolation of the dialkylaminomethyleneindolizinium perchlorate intermediate. The crude aldehyde was obtained by refluxing or steam-distillation of the resulting alkaline mixture.

CVI (a) Condensation of 3-Ethoxymethyleneindolizinium Perchlorates with N-Methylaniline.

CVI $(a)_1$ 3-Ethoxymethylene-2-methylindolizinium perchlorate with N-methylaniline.

A mixture of 3-ethoxymethylene-2-methylindolizinium perchlorate (0.574g, 0.002 mole), N-methylaniline (0.5 mls, ≏ 0.005 mole) and methanol (5 mls) was refluxed for 2 minutes. The resulting dark blue solution on cooling deposited needles of 2-Methyl-3-(N-methyl-N-phenylaminomethylene)indolizinium perchlorate (0.21 g, 50%). These were collected washed with a little methanol, followed by ether and recrystallised from methanol, m.p. > 340° with slow decomp. > 280°.

Found N = 7.63 $C_{17}H_{17}ClN_2O_4$ requires N = 8.03

CVI (a)$_2$ 3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate with N-methylaniline.

A mixture of 3-ethoxymethylene-1,2-dimethylindolizinium perchlorate (0.603 g, 0.002 mole), N-methylaniline (0.6 mls, ≏ 0.006 mole) and methanol (10 mls) was refluxed for 2 minutes. The resulting dark green solution on cooling deposited greenish-black microcrystals of 1,2-dimethyl-3-(N-methyl-N-phenylaminomethylene) indolizinium perchlorate (0.327 g, 45%). These were collected, washed with a little methanol, followed by ether, and after recrystallisation from methanol had m.p. > 340° (Transition from microcrystals to large needles on block preheated to 280°).

Found N = 7.90 $C_{18}H_{19}ClN_2O_4$ requires N = 7.72

CVI (b) Condensation of 3(1)-Ethoxymethyleneindolizinium Perchlorates with Diethylamine followed by Alkaline Hydrolysis of the resulting Diethylaminomethyleneindolizinium Perchlorates to the corresponding Indolizine Aldehydes.

CVI $(b)_1$ The transient 3-ethoxymethyleneindolizinium perchlorate

Ethyl orthoformate (15 mls, 0.09 mole) was added to a cooled solution of indolizinium perchlorate (2.17 g, 0.01 mole). After 1 minute, allowed for the completion of the formation of 3-ethoxymethyleneindolizinium perchlorate and partial formation of monomethine dye, diethylamine (2.0 mls, $\simeq$ 0.02 mole) was added to give a redish-brown solution. To this was added aqueous sodium hydroxide (50 mls, 10% (w/w)), and the resulting mixture was refluxed for 1 hour, cooled and extracted several times with ether. The ether extract was washed well with water, dried (Na_2SO_4) and the extract was evaporated. The residual dark redish-brown oil was taken up in a little petroleum ether (60 - 80°). The resulting solution after being filtered and cooled, deposited yellow crystals which rapidly turned violet-brown, making isolation of the pure 3-formylindolizine impossible. The infra red spectrum of the yellow crystals in carbon tetrachloride showed twin carbonyl peaks with the main peak at ν = 1644 cm^{-1} (μ = 6.085).

CVI $(b)_2$ 3-Ethoxymethylene-2-methylindolizinium perchlorate

A mixture of 3-ethoxymethylene-2-methylindolizinium perchlorate (1.208 g, 0.004 mole), diethylamine (2.0 mls, $\simeq$ 0.02 mole) and methanol (2 mls) was gently warmed for a few minutes. To the resulting blue oil of the diethylaminomethylene intermediate was added aqueous sodium hydroxide (100 mls, 10% ($^w/_w$)) and the resulting mixture was steam-distilled. The light green distillate deposited cream-white needles of 3-formyl-2-methylindolizine (0.243 g, 38.8%) on cooling. These were collected and sublimed at 15 mm (block temperature 125°). The sublimate recrystallised from petroleum ether (40 - 60°) as cream-white needles which slowly turn faint green on standing, m.p. 57.5° (lit.[112] m.p. 56.5 - 57.5°).

CVI (b)$_5$ <u>3-Ethoxymethylene-1,2-dimethylindolizinium perchlorate. Condensation with diethylamine.</u>

A mixture of 3-ethoxymethylene-1,2-dimethylindolizinium perchlorate (1.206g, 0.004 mole), diethylamine (2.0 mls, 0.02 mole) and methanol (5 mls) was refluxed for a few minutes. The resulting dark green solution on cooling deposited microcrystals of <u>1,2-Dimethyl-3-(NN-diethylaminomethylene)indolizinium perchlorate</u> (0.98 g, 75%). These were collected, washed with a small volume of methanol, then with ether and recrystallised from methanol, m.p. > 340° [transition from microcrystals to needles > 245° (preheated block)].

Found N = 8.80 $C_{15}H_{17}ClN_2O_4$ requires N = 8.52

<u>Alkaline hydrolysis of 1,2-Dimethyl-3-(NN-diethylaminomethylene)-indolizinium perchlorate to 3-formyl-1,2-dimethylindolizine.</u>

Aqueous sodium hydroxide (75 mls, 10% ($^w/_w$)) was added to 1,2-dimethyl-3-(NN-diethylaminomethylene)indolizinium perchlorate(0.987g, 0.003 mole) and the resulting mixture was steam-distilled. The light green distillate deposited cream needles of 3-formyl-1,2-dimethylindolizine (0.315 g, 80%) (45% from ethoxymethylene compound). These were collected, sublimed at 15 mm (block temperature 150°), and on recrystallisation from petroleum ether (40 - 60°) gave cream needles, m.p. 79 - 80°.

Found C = 75.97 H = 6.48

$C_{11}H_{11}NO$ requires C = 76.27 H = 6.40

3-Formyl-1,2-dimethylindolizine was obtained in higher yield (57%) from 3-ethoxymethylene-1,2-dimethylindolizinium perchlorate without isola tion of the intermediate aminomethyleneindolizinium perchlorate.

CVI (b)$_4$ 1-Ethoxymethylene-2,3-dimethylindolizinium perchlorate.

A mixture of 1-ethoxymethylene-2,3-dimethylindolizinium perchlorate (1.208 g, 0.004 mole), diethylamine (2.0 mls, 0.02 mole), and methanol (2 mls) was warmed for a few minutes. To the resulting diethylaminomethylene intermediate was added aqueous sodium hydroxide (100 mls, 10% (w/w)) and this mixture was refluxed for 30 minutes. Yellow-brown needles of crude 1-formyl-2,3-dimethylindolizine (0.604 g) deposited. These were collected, washed with water, and recrystallised from petroleum ether (60 - 80°)as pale yellow needles (0.408 g, 59%) m.p. 90 - 93° (lit.[112] m.p. 94 - 95° yield 36%). Found C = 76.30 H = 6.38

$C_{11}H_{11}NO$ requires C = 76.27 H = 6.40

CVI (b)$_5$ <u>3-Ethoxymethylene-2,6-dimethylindolizinium perchlorate.</u>

A mixture of 3-ethoxymethylene-2,6-dimethylindolizinium perchlorate (1.208 g, 0.004 mole), diethylamine (2.0 mls, ≏ 0.02 mole) and methanol (2 mls) was warmed for a few minutes. Aqueous sodium hydroxide (100 mls, 10% (w/w)) was added and the resulting mixture was steam-distilled. The yellowish-green distillate on cooling deposited yellow needles of <u>3-formyl-2,6-dimethylindolizine</u> (0.232 g, 33.5%) which were collected, sublimed at 15 mm (block temperature 130°) and recrystallised from petroleum ether (40 - 60°). The aldehyde formed large, pale yellow needles, m.p. 70 - 71.5°.

Found C = 75.96 H = 6.34

$C_{11}H_{11}NO$ requires C = 76.27 H = 6.40

CVI (b)$_6$ <u>3-Ethoxymethylene-2,8-dimethylindolizinium perchlorate.</u>

A mixture of 3-ethoxymethylene-2,8-dimethylindolizinium perchlorate (1.209 g, 0.004 mole), diethylamine (2.0 mls, ≏ 0.02 mole) and methanol (2 mls) was warmed for a few minutes. To the resulting diethylaminomethylene intermediate was added aqueous sodium hydroxide (100 mls, 10% (w/w)) and the resulting mixture steam-distilled. The light green distillate on cooling deposited yellow needles of <u>3-formyl-2,8-dimethylindolizine</u> (0.489 g, 70%) which were collected, sublimed at 15 mm (block temperature 135°). Recrystallisation from petroleum ether (60 - 80°) gave pale yellow needles, m.p. 91 - 93.5°.

Found C = 76.66 H = 6.30 N = 8.09

$C_{11}H_{11}NO$ requires C = 76.27 H = 6.40 N = 8.09

CVI $(b)_7$ 1-Ethoxymethylene-3-ethyl-2-methylindolizinium perchlorate.

A mixture of 1-ethoxymethylene-3-ethyl-2-methylindolizinium perchlorate (1.260 g, 0.004 mole), diethylamine (2.0 mls, ≏ 0.02 mole) and methanol (2 mls) was warmed for a few minutes and to the mixture aqueous sodium hydroxide (100 mls, 10% ($^w/_w$)) was added. The resulting mixture was steam-distilled. Oily drops which came over with the pale green distillate crystallised on being thoroughly cooled, giving yellow needles of 1-formyl-3-ethyl-2-methylindolizine (0.382 g, 51%). These were collected, sublimed at 15 mm (block temperature 135°) and on recrystallisation from petroleum ether (40 - 60°) gave clear, pale yellow needles, m.p. 99 - 100.5°.

Found N = 7.06 $C_{12}H_{13}NO$ requires N = 7.48

CVI $(b)_8$ 3-Ethoxymethylene-2-phenylindolizinium perchlorate

Ethyl orthoformate (15 mls, 0.09 mole) was added to a solution of 2-phenylindolizinium perchlorate (2.94 g, 0.01 mole) in acetonitrile (20 mls). Solvent was removed under reduced pressure from the resulting green solution, leaving a green oil to which diethylamine (2.0 mls, ≏ 0.02 mole) was added. A reddish orange oil formed. Aqueous sodium hydroxide (100 mls, 10% ($^w/_w$)) was added and the resulting mixture was refluxed for 1 hour. The brown oil which had formed solidified on cooling to give the crude 3-formyl-2-phenyl-indolizine (1.21 g). Recrystallisation from petroleum ether (60 - 80°) gave clear off-white needles, (0.91 g, 41% from perchlorate), m.p. 99.5 - 104°.

Found C = 81.24 H = 5.28 N = 6.66

$C_{15}H_{12}NO$ requires C = 81.06 H = 5.44 N = 6.31

CVI $(b)_9$ <u>3-Ethoxymethylene-1-methyl-2-phenylindolizinium perchlorate</u>

A mixture of 3-ethoxymethylene-1-methyl-2-phenylindolizinium perchlorate (1.456 g, 0.004 mole), diethylamine (2.0 mls, ≏ 0.02 mole) and methanol (2 mls) was warmed for a few minutes. Aqueous sodium hydroxide (100 mls, 10% (w/w)) was added and the resulting mixture was refluxed for 1 hour, cooled, and extracted several times with ether. The ether extracts were washed well with water and dried (K_2CO_3). Evaporation of the ether left a light brown solid consisting of the crude <u>3-formyl-1-methyl-2-phenylindolizine</u> (0.915 g). This was sublimed at 15 mm. (block temperature 150°) and recrystallised from ethanol to give the pure aldehyde (0.628 g, 70.5%) as silky needles, m.p. 119.5 - 121°.

Found C = 81.68 H = 5.56 N = 5.95

$C_{16}H_{13}NO$ requires C = 81.67 H = 5.57 N = 5.95

CVI $(b)_{10}$ <u>3-Ethoxymethylene-2-methyl-1-phenylindolizinium perchlorate</u>.

A mixture of 3-ethoxymethylene-2-methyl-1-phenylindolizinium perchlorate (1.456 g, 0.004 mole), diethylamine (2.0 mls, ≏ 0.02 mole) and methanol (2 mls) was warmed for a few minutes. Aqueous sodium hydroxide (100 mls, 10% (w/w)) was added and the resulting mixture was refluxed for 30 minutes, cooled and extracted several times with ether. The ether extracts were washed well with water and dried (K_2CO_3).

Evaporation of the ether left a brown oil which solidified on cooling to give the crude <u>3-formyl-2-methyl-1-phenylindolizine</u> (0.435 g). This was distilled at 15 mm. (block temperature 200°) and recrystallised from cyclohexane to give the pure aldehyde (0.371 g, 39%) as cream needles, m.p. 93.5 - 95°.

Found C = 81.72 H = 5.71

$C_{16}H_{13}NO$ requires C = 81.67 H = 5.57

CVI (b)$_{11}$ <u>1-Ethoxymethylene-3-methyl-2-phenylindolizinium perchlorate</u>

A mixture of 1-ethoxymethylene-3-methyl-2-phenylindolizinium perchlorate (1.456 g 0.004 mole), diethylamine (2.0 mls, ≏ 0.02 mole) and methanol (2 mls) was warmed for a few minutes. Aqueous sodium hydroxide (100 mls, 10% (w/w)) was added and the resulting mixture refluxed for 1 hour, cooled, and extracted several times with ether. The ether extracts were washed well with water and dried (K_2CO_3). Evaporation of the ether left a bright yellow crystalline mass of the crude <u>1-formyl-3-methyl-2-phenylindolizine</u> (0.728 g). This was sublimed at 15 mm. (block temperature (180°) and recrystallised from ethanol to give the pure aldehyde (0.48 g, 51%) as pale yellow prismatic needles, m.p. 154 - 156°.

Found C = 81.50 H = 5.45 N = 5.99

$C_{16}H_{13}NO$ requires C = 81.67 H = 5.57 N = 5.95

CVI (b)$_{12}$ 1-Ethoxymethylene-5-methyl-2-phenylindolisinium perchlorate

A mixture of 1-ethoxymethylene-5-methyl-2-phenylindolisinium perchlorate (1.456 g, 0.004 mole), diethylamine (2.0 mls, ≙ 0.02 mole) and methanol (3 mls) was warmed for a few minutes. Aqueous sodium hydroxide (100 mls, 10% (w/w)) was added and the resulting solution refluxed for 30 minutes, cooled, and the brown solid of 1-formyl-5-methyl-2-phenylindolisine (0.884 g) which had formed was collected, washed with water, dried, and recrystallised from cyclohexane to give pure aldehyde (0.645 g, 68%) as silky needles, m.p. 106.5 - 108.5°

Found N = 6.32 $C_{16}H_{13}NO$ requires N = 5.96

CVII Reaction of Indolisines and Di-indolisinylmethanes with Triphenylmethyl Perchlorate.[144]

CVII$_1$ Indolisine with triphenylmethyl perchlorate.

A solution of indolisine (4.68 g, 0.04 mole) in acetonitrile (5 mls) was added to a solution of triphenylmethyl perchlorate (13.68 g, 0.04 mole) in acetonitrile (10 mls). The colour of the triphenylmethyl perchlorate disappeared leaving a pale green solution from which on cooling white crystals of Bis-1,3-ditrityl-indolisine (3.168 g, 33%) deposited on cooling. These were collected, washed with a little acetonitrile followed by ether and after recrystallisation from methanol, formed colourless needles, m.p. 259.5 - 262°.

Found C = 91.58   H = 5.70   N = 2.62

$C_{46}H_{35}N$ requires C = 91.81   H = 5.86   N = 2.33

CVII$_2$ <u>2-Methylindolizine with triphenylmethyl perchlorate.</u>

A solution of 2-methylindolizine (2.62 g, 0.02 mole) in acetonitrile (5 mls) was added to a solution of triphenylmethyl perchlorate (6.86 g, 0.02 mole) in warm acetonitrile (30 mls). The colour of the triphenylmethyl perchlorate disappeared leaving a pale green solution from which colourless needles of <u>2-methyl-1-tritylindolizinium perchlorate</u> (2.305 g, 24.5%) deposited on cooling. These were collected, washed with a little acetonitrile followed by ether and recrystallised from acetonitrile as colourless needles, m.p. 215.5 - 216°.

Found N = 3.33 $C_{28}H_{24}ClNO$ requires N = 2.96

CVII$_3$ <u>Hydrolysis of 2-methyl-3-tritylindolizinium perchlorate.</u>

Aqueous sodium hydroxide (15 mls, 20% ($^{w}/_{w}$)) was added to a solution of 2-methyl-3-tritylindolizinium perchlorate (0.473 g, 0.001 mole) in acetonitrile (5 mls), and the resulting mixture was refluxed for 10 minutes. The precipitated <u>2-methyl-1-tritylindolizine</u> (0.346 g, 93%) was collected, washed with water and dried. Recrystallisation from acetonitrile gave clear pale yellow prisms, m.p. 194.5 - 198.5° (d)

Found N = 3.79 $C_{28}H_{23}N$ requires N = 3.75

CVII$_4$ <u>1,2-Dimethylindolisine with triphenylmethyl perchlorate.</u>

A solution of 1,2-dimethylindolisine (1.45 g, 0.01 mole) in acetonitrile (5 mls) was added to a solution of triphenylmethyl perchlorate (3.43 g, 0.01 mole) in warm acetonitrile (20 mls). The colour of the triphenylmethyl perchlorate disappeared leaving a pale green solution from which colourless needles deposited on cooling; a further deposition occurred on the addition of ether to the mother liquors. The combined crops of <u>1,2-dimethyl-3-tritylindolisinium perchlorate</u> (1.432 g, 30.0%) were washed with water followed by ether and recrystallised from acetonitrile giving colourless needles, m.p. 163 - 165° (softening and turning green > 155°).

CVII$_5$ <u>Hydrlysis of 1,2-dimethylindolisinium perchlorate.</u>

Aqueous sodium hydroxide (15 mls, 20% (w/w)) was added to a solution of 1,2-dimethylindolisinium perchlorate (0.245 g, 0.005 mole) in acetonitrile (5 mls), and the resulting mixture was refluxed for 10 minutes. The precipitated <u>1,2-dimethyl-3-tritylindolisine</u> (0.175 g, 90%) was collected, washed with water and dried. Recrystallisation from acetonitrile gave cream needles, m.p. 187 - 190°.

Found C = 90.19 H = 6.41

$C_{29}H_{25}N$ requires C = 89.91 H = 6.50

CVII$_6$ 1,1'2,2'-Tetramethylmethylene-3,3'-di-indolizine with triphenylmethyl perchlorate

Triphenylmethyl perchlorate (1.026 g, 0.003 mole) was added to a solution of 1,1'2,2'-tetramethylmethylene-3,3'-di-indolizine (0.906 g, 0.003 mole) in glacial acetic acid (30 mls). The resulting solution on being refluxed developed an intensely dark blue colour and deposited dark blue crystals which were collected. The mother liquors were refluxed for a further 2hours, cooled and a further small crop of blue crystals collected. The combined crops (0.878 g) (λ max. 602) were washed with a little glacial acetic acid and petroleum ether (40 - 60^o).

The filtrate and washings were poured into petroleum ether (40 - 60^o) (500 mls), and the resulting solution was extracted several times with water until the blue colour was completely removed from the petrol layer. The petrol-ether layer was then extracted several times with concentrated sulphuric acid, to remove triphenylcarbinol, and finally washed free from acid with water before being dried (K_2CO_3). The bulk of the petrol-ether was evaporated, and the residue on being chromatographed gave triphenylmethane (0.716 g, 98%), m.p. 91.5 - 93^o.

CVIII Reaction of Indolizines and Di-indolizinylmethanes with High potential Quinones.

Introduction

Chloranil, 2,3,5,6 - tetrachloro-1,4-benzoquinone (C.A.) was recrystallised from glacial acetic acid or benzene. 2,5-Dicyano-quinol, 2,3-dicyano-1,4-benzoquinone (D.C.Q.) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (D.D.Q.) were prepared by the method of Creighton and Jackman[145] The following procedure was adopted for the preparation of 3,4,5,6 - tetrachloro-1,2-benzoquinone (T.B.Q.).

Catechol(50.0 g) in glacial acetic acid (250 mls) was added to a three-necked flask fitted with stirrer, condenser, a wide bore gas inlet tube and thermometer. Chlorine gas dried by passage through sulphuric acid was passed at such a rate that the temperature of the solution remained between 25 - 30°. After several hours solid started to precipitate, and when no more hydrogen chloride was evolved, but rather the chlorine passed out of the solution, the precipitated tetrachlorocatechol (94 g, 87%) was collected, washed with a little glacial acetic acid and recrystallised from glacial acetic acid, the product was finally washed with a little petrol and dried.

A solution of tetrachlorocatechol (94 g) in ethanol (150 mls) at room temperature was added to a vigorously stirred solution of concentrated nitric acid (18 mls, S.G. 1.42) in glacial acetic acid.

The solution turned red, then deep-red, and finally bright red again. Stirring was continued for 15 mins. from the start of the reaction. Ice cold water was then added; 3,4,5,6-tetrachloro-1,2-benzoquinone crystallised at once as dark red crystals. The solution was stirred for a further 15 minutes, then filtered, and the precipitate washed well with water, dried and recrystallised from the minimum volume of carbon tetrachloride.

CVIII$_1$ 2,3-Dimethylindolizine with chloranil.

Chloranil (1.25 g, 0.01 mole) was added to a solution of 2,3-dimethylindolizine (1.45 g 0.01 mole) in methanol (80 mls). The resulting intense blue solution was refluxed for 2 minutes, allowed to cool, and poured into ether (1,000 mls). The ether solution was then extracted several times with water, then with alkali. The alkaline extract was filtered and acidified, and the precipitated quinol was extracted with ether. The ether extract was washed with water, dried (Na_2SO_4), and the ether evaporated leaving crude 2,3,5,6-tetrachloro quinol (0.248 g, 20%) as a brown residue. This was crystallised with charcoal screening from a small volume of glacial acetic giving the pure quinol (0.190 g, 16%) as colourless needles m.p. 234 - 236°, with sublimation > 200°; lit.[146] m.p. 231°.

CVIII$_2$ 1,2,3-Trimethylindolizine with chloranil.

Chloranil (1.23 g, 0.0005 mole) was added to a solution of 1,2,3-trimethylindolizine (1.59 g, 0.01 mole) in glacial acetic acid (20 mls). The solution became dark green in reflected and red in transmitted light, while deposition of quinol occurred. The solution was left with intermittent swirling for 8 hours and then poured into ether (400 mls). The ether solution was washed with water before being extracted several times with alkali. The alkaline extract was acidified, and the precipitated quinol was extracted into ether. The ether extract was washed and dried (Na_2SO_4) before evaporation of solvent. Crude quinol (1.005 g, 82%) which remained was recrystallised from glacial acetic acid. The pure quinol (0.814 g, 67%) was obtained as colourless needles, m.p. 234 - 236°, with sublimation > 200°.

The above procedure was repeated using methanol as solvent. 1,2,3 Trimethylindolizine (1.59 g, 0.01 mole) and 2,3,5,6-tetrachloro-1,4-benzoquinone (1.23 g, 0.005 mole) gave crude quinol (0.804 g, 66%) which after recrystallisation from acetic acid gave the pure quinol (0.595 g, 49%), m.p. 234 - 236°, with sublimation > 200°.

Reaction of Di-indolizinylmethanes with High Potential Quinones

The reactions were carried out in methanol or acetonitrile solutions. The effect of varying the solvent, reaction time, and proportions of the reactants was studied in the reactions of quinones with 1,1'2,2'-tetramethylmethylene-3,3'-di-indolizine. The experimental procedure adopted for these reactions is exemplified by reference to the reaction between 1,1'2,2'-tetramethylmethylene-3,3'-di-indolizine and chloranil using (a) methanol as solvent [CVIII$_3$], where the yield of monomethine dye is favoured and (b) acetonitrile as solvent [CVIII$_4$] where the yield of green dye salt is favoured.

Details of all other dehydrogenations involving 1,1'2,2'-tetramethylmethylene-3,3'-di-indolizine are summarised in $CVIII_6$. Details of the reactions involving other di-indolizinylmethanes and 2,3,5,6- and 3,4,5,6,-tetrachloro-1,4- and 1,2-benzoquinones, using equimolecular proportions of reactants and a standard reaction time of 15 minutes, are summarised in $CVIII_7$.

$CVIII_5$ __1,1'2,2'-Tetramethylmethylene-3,3'-di-indolizine with chloranil in methanol in the presence of perchloric acid.__

Chloranil (1.23 g, 0.005 mole) in methanol (50 mls) was added to a suspension of 1,1'2,2'-tetramethylmethylene-3,3'-di-indolizine in boiling methanol (80 mls). The solution became deep blue and was refluxed for 2 minutes. Perchloric acid (2 mls) was added, and the solution was refluxed for a further 2 minutes, set aside for a few minutes to cool, and filtered. A small green crystalline residue of the __green dye salt__ ((26)A) (0.249 g, 12%) was collected, washed with a little methanol followed by ether, and recrystallised from acetonitrile. It formed black needles which slowly decompose $\not>$300°; λ max. (acetonitrile) 389 (4.60) 860 (broad) (3.44).

Found C = 62.85 H = 5.04 N = 7.15 Cl = 9.09

$C_{21}H_{19}ClN_2O_4$ requires C = 63.24 H = 4.80 N = 7.02 Cl = 8.89

The methanolic mother liquors remaining after filtration of the green dye salt were thoroughly cooled. The blue-black crystals of 3-(1,2-dimethylindolizin-3-yl) methylene-1,2-dimethylindolizinium perchlorate (1.245 g, 61%) which had deposited, were collected, washed with ether and recrystallised from ethanol forming blue-black microcrystals (0.841 g 45%) which slowly melted with decomposition >259°; λ max. (methanol containing 2% (%) perchloric acid) 629 (4.61).

After filtration of the blue monomethine dye salt, a sodium hydroxide solution (200 mls, 10% (%)) was added to the mother liquors, and the resulting mixture was shaken for 2 hours, then extracted several times with ether. The alkaline layer was filtered, poured into an excess of hydrochloric acid, and the precipitated quinol extracted with ether. The ether extract was washed with water, dried (Na_2SO_4). Evaporation of the ether left crude 2,3,5,6-tetrachloro-1,4-quinol (0.803 g 65%) as a light brown crystalline residue which recrystallised from a small volume of glacial acetic acid as large white needles m.p. 234 - 236° (sublimation >200°).

$CVIII_4$ <u>1,1'2,2'-Tetramethylmethylene-3,3'-di-indolizine with Chloranil in acetonitrile in the presence of perchloric acid.</u>

A suspension of chloranil (2.46 g)(0.01 mole) in acetonitrile (50 mls) was added to a solution of 1,1'2,2'-tetramethylmethylene-3,3'-di-indolizine (3.02 g, 0.01 mole) in acetonitrile (60 mls). An intense green blue colour developed and precipitation of the brown quinolate occurred. After the mixture had been refluxed for 15 mins. perchloric acid (2.5 mls) was added. The mixture refluxed for a further 15 minutes, set aside to cool for a few minutes, and filtered. The crystalline precipitate of <u>green dye salt</u> ((26)A) (1.264 g, 32%) was collected, washed with a little acetonitrile then ether, and recrystallised from acetonitrile. It formed greenish black needles which slowly decomposed > 300°; λ max. (acetonitrile) 589 and 860 (broad), identical with the product of the preceeding experiment.

Sodium hydroxide solution (200 mls, 10% (w/w)) was added to the mother liquors. The mixture was shaken for 2 hours, then extracted with ether. The alkaline layer was filtered poured into an excess of hydrochloric acid, and the precipitated quinol was extracted into ether. The ether extract washed with water, dried (Na_2SO_4), and the solvent was evaporated. The residual crude quinol (1.644 g, 85%), a light brown crystalline residue, was recrystallised from a small volume of glacial acetic acid and obtained as white needles, m.p. 254 - 256° (sublimation > 200°).

CVIII$_5$ <u>1,1'2,2'-Tetramethylmethylene-3,3'-di-indolizine with Chloranil in acetonitrile, isolation and treatment of the quinolate with perchloric acid.</u>

A suspension of chloranil (0.615 g, 0.0025 mole) in acetonitrile (20 mls) was added to a warmed solution of 1,1'2,2'-tetramethylmethylene-3,3'-di-indolizine (0.76 g, 0.0025 mole) in acetonitrile (30mls). Development of an intense green-blue colour was accompanied by the formation of a brown precipitate. The mixture was refluxed for 15 minutes. The precipitated <u>quinolate</u> ((26)B) (0.610 g, 45%) was collected, washed with a little acetonitrile, then with much ether, and on recrystallisation from acetonitrile formed brown microcrystals m.p. 247 - 257° (d) λ max. (acetonitrile) 589.1 and 840

The brown quinolate (0.545 g, 0.001 mole) in methanol (50 mls) was treated with perchloric acid (0.4 mls) and the small green needles of green dye salt (0.245g, 61%) which precipitated at once were collected, washed with a little methanol followed by ether, and recrystallised from acetonitrile. It formed dark green needles which decomposed > 300°; λ max. (acetonitrile) 389 and 860 (broad), identical with the products of the two preceeding experiments.

Ether (200 mls) was added to the methanol-ether liquors and the resulting mixture was washed well with water before being dried (Na_2SO_4). Evaporation of the ether left a grey white residue of the crude quinol (0.232 g, 98%) which after recrystallisation from a small volume of glacial acetic acid formed white needles (0.185, 78%), m.p. 234 - 236° (sublimation > 200°).

$CVIII_6$

QUINONE	MOLES METHANE	MOLES QUINONE	SOLVENT	REFLUX TIME Mins.	% YIELD PPTD. PRODUCT	λ MAX	M.p.	% RECOVERY QUINOL
T.B.Q.	0.005	0.005	CH_3OH	2	mono-methine dye 39%	629	melting with dec.250°	16%
T.B.Q.	0.005	0.005	CH_3OH	15	mono-methine dye 42% green dye salt 4.8%	629 389 860	melting with dec 258 slow dec >300°	19.8%
T.B.Q.	0.01	0.01	CH_3OH	15	green dye salt 30%	389 860	slow dec >300°	20%
C.A	0.005	0.005	CH_3OH	2	mono-methine dye 62% green dye salt 12%	629 389 860	melting with dec 260° slow dec >300°	65%
C.A	0.005	0.005	CH_3CN	15	mono-methine dye 40% green dye salt 16%	629 389 860	melting with dec 250° slow dec >300°	63%
C.A	0.0025	0.0025	CH_3CN	15	Quinolate 45% green dye salt 28%	389 840	247-257° slow dec >300°	98%
C.A	0.005	0.005	CH_3CN	15	green dye salt 31.5	389 860	slow dec >300°	65%

$CVIII_{a}$ continued

QUINONE	MOLES METHANE	MOLES QUINONE	SOLVENT	REFLUX TIME Mins.	% YIELD PPTD. PRODUCT	λ MAX	M.p.	% RECOVERED QUINOL
C.A	0.005	0.01	CH_3CN	15	green dye salt 37%	389 860	slow dec > 300°	
D.C.Q.	0.01	0.01	CH_3CN	15	green dye salt 17.5%	389 860	slow dec > 300°	72%
D.D.Q.	0.0002	0.0002	CH_3CN	15	green dye salt 3.5% mono-methine dye 1%	389 860 629	slow dec > 300° melting with dec 282°	16.0%

CVIII,7

DI-INDOLIZINYL METHANE	QUINONE	SOLVENT	λ max of PRECIPITATE or SOLUTION	M.p. PRECIPITATE	M.p. & λ max CORRESPONDING MONO-METHINE DYE
2,2'-Dimethyl-methylene-3,3'-di-indolizine	T.B.Q.	CH_3CN	588		582
	C.A	CH_3CN	595 broad		
12,2'-Trimethyl-methylene-3,3'-di-indolizine	C.A	CH_3CN	592		593
	C.A	Methanol	611		
2,2'3,3'-Tetramethyl-methylene-1,1'-di-indolizine	C.A	Methanol	584	195-210°	586
					M.p 260-270.5
	C.A	CH_3CN	584.5		
	T.B.Q.	Methanol	584	190-205°	
2,2'-Dimethyl-1,1'-diphenyl-methylene-3,3'-di-indolizine	T.B.Q	CH_3CN	642.5		643
	C.A	Methanol	642.5		

CVIII$_8$ <u>Sodium borohydride reduction of 'green dye salt' to 'red base'</u>.

To a stirred suspension of green dye salt (0.800 g, 0.002 mole) in methanol (50 mls) was added, portionwise, a total of (2.5 g) of sodium borohydride over about 1 hour, the solution turning from green to crimson-red with the precipitation of crimson-red needles of <u>red base (37)</u> (0.575 g, 96%). These were collected, washed thoroughly with water, with a little methanol (5 mls), dried in vacuo, and recrystallised from a small volume of benzene (or acetonitrile) as long crimson-red needles (0.245 g, 41%) which decolourised to black needles at 152.5 - 155^{o} with slight slow melting > 215^{o}, λ max. (acetonitrile) 514 (3.82) λ max. (glacial acetic acid) 560 (3.81).

Found C = 84.59 H = 6.52 N = 9.11

$C_{21}H_{20}N_2$ requires C = 83.96 H = 6.71 N = 9.55

CVIII$_9$ <u>Action of an excess of perchloric acid on the red base.</u>

Perchloric acid (0.4 mls) was added to a solution of the red base (0.20 g) in acetonitrile (5 mls). The resulting yellow-brown solution was heated to the boiling point, filtered, and on cooling deposited large colourless prismatic needles of the <u>diperchlorate</u> ((39)A) (0.328g, 98%). These were collected, washed with ether, and after being recrystallised from acetonitrile containing 1% (X) perchloric acid formed colourless prismatic needles which became opaque at 142 - 152^{o} and slowly decompose > 152^{o}, becoming brownish yellow up to 255^{o} with more rapid decomposition > 255^{o}.

Found C = 51.00 H = 4.38 N = 5.38

$C_{21}H_{22}Cl_2N_2O_8$ requires C = 50.31 H = 4.42 N = 5.59

CVIII$_{10}$ Solvolysis of the 'diperchlorate' by ethanol.

A solution of the 'diperchlorate' 0.3 g in ethanol (5 mls) heated to the boiling-point, became crimson-violet and was filtered hot. The cooled filtrate deposited rhombic bronze-red plates of the monoperchlorate (28) (0.165 g, 69%). These were collected, washed with a little ethanol, followed by ether and recrystallised from ethanol. Bronze-red plates were obtained which slowly decompose 240°, max. (acetonitrile) 558 (5.87).

Found C = 62.29 H = 5.18 N = 7.16

$C_{21}H_{21}ClN_2O_4$ requires C = 62.92 H = 5.36 N = 6.99

CVIII$_{11}$ Quinone dehydrogenation of the red base in the presence of perchloric acid.

A mixture of the red base (0.300 g. 0.001 mole), chloranil (0.246 g, 0.001 mole) and acetonitrile (20 mls) was refluxed for 5 minutes. A brown solid precipitated from the brownish yellow solution. Perchloric acid (0.5 mls) was added and the solution boiled for a further 5 minutes then cooled and filtered. The salt (0.300 g. 75%) which crystallised was collected, dried and recrystallised from acetonitrile. It was identical with the green dye salt product isolated from the dehydrogenation of 1,1'2,2'-tetramethylmethylene-3,3 di-indolizine with chloranil and perchloric acid.

CIX <u>Condensation of Indolisinium Perchlorates with Glyoxal</u>

CIX$_1$ <u>1,2-Dimethylindolisinium perchlorate with glyoxal in acetonitrile</u>.

Glyoxal (30% w/w) (3 ml ~ 0.015 mole) was added to a hot solution of 1,2-dimethylindolisinium perchlorate (2.457 g, 0.01 mole) in acetonitrile (20 mls). The solution was refluxed for 2 minutes, cooled, and perchloric acid (2 mls) was added. After a further 30 minutes cooling the <u>ethanediylidenebis-(1,2-dimethylindolisinium perchlorate</u>) (35) (0.810 g, 32%) which had deposited, was collected, washed with a little acetonitrile followed by acetonitrile-ether (1:1), then with ether. It recrystallised from acetonitrile as red brown prisms which melted slowly with dec. > 225° ; λ max. (acetonitrile containing 2% (v/v) perchloric acid) 365 (4.31) 512 (4.29).

Found C = 51.58 H = 4.46 N = 5.32

$C_{22}H_{22}Cl_2N_2O_8$ requires C = 51.48 H = 4.32 N = 5.46

CIX$_2$ <u>2,3-Dimethylindolisinium perchlorate with glyoxal in acetonitrile</u>.

Glyoxal (30% w/w)(3ml ~ 0.015 mole) was added to a hot solution of 2,3-dimethylindolisinium perchlorate (2.457 g, 0.01 mole) in acetonitrile (10 mls). The solution was refluxed for 2 minutes, cooled, and perchloric acid (2 mls) was added. After a further 30 minutes cooling the <u>ethanediylidenebis-(2,3-dimethylindolisinium perchlorate</u>) (36) (0.54 g, 21%) which had deposited, was collected, washed successively with a little acetonitrile, acetonitrile-ether (1:1) and with ether, and recrystallised from acetonitrile containing

1% ($^{v}/_{v}$) of perchloric acid. It formed small brown prismatic needles which slowly decomposed > 260°; λ max. (acetonitrile containing 2% ($^{v}/_{v}$) perchloric acid) 460 (4.54).

Found C = 51.76 H = 4.57 N = 5.08

$C_{22}H_{22}Cl_2N_2O_8$ requires C = 51.48 H = 4.32 N = 5.46

CIX_3 1-Methyl-2-phenylindolizinium perchlorate with glyoxal in glacial acetic acid.

Glyoxal (30% $^{w}/_{w}$) (3 mls ~ 0.015 mole) was added to a hot solution of 1-methyl-2-phenylindolizinium perchlorate (3.07 g, 0.01 mole) in glacial acetic acid (40 mls). The solution was refluxed for 2 minutes, cooled, and perchloric acid (2 mls) was added. After a further 30 minutes cooling the ethanediylidenebis-(1-methyl-2-phenylindolizinium perchlorate) (37) (1.330 g, 42%) which had deposited, was collected, washed with a little glacial acetic acid, with ether, dried and recrystallised from glacial acetic acid containing 1% ($^{v}/_{v}$) perchloric acid as ruby coloured prisms which slowly decomposed > 210° with melting 245 - 255°; λ max. (acetonitrile containing 2% perchloric acid). 248 (broad) (4.40) 368 (broad) (4.16) 505 (4.20).

Found C = 60.55 H = 4.12 N = 4.14

$C_{32}H_{26}Cl_2N_2O_8$ requires C = 60.29 H = 4.11 N = 4.39

CIX$_6$ 1,2-Dimethylindolizinium perchlorate with glyoxal in ethanol.

To a boiling solution of 1,2-dimethylindolizinium perchlorate (4.92 g 0.02 mole) in ethanol(120 mls) was added glyoxal (30% $^w/_w$) (6.0ml ~ 0.03 mole). The mixture became blue and was heated at the boiling point for 30 seconds or until the product began to crystallise from the deep blue solution. The product was filtered, washed with ethanol (60 ml) and the combined filtrates were filtered, diluted with ether (100 ml) and set aside for 24 hours. 3-(1,2-dimethylindolizin-3-yl)methylene-1,2-dimethylindolizinium perchlorate (0.22 g, 5.5%) was collected as violet black rosettes of crystals with a green golden reflex. M.p. > 261° with dec., λ max. (methanol containing 2% perchloric acid) 630.

Washing of the initial product was continued with hot ethanol until the colour of the filtrates had changed from blue to violet. The solid was extracted with boiling ethanol (5 X 150 ml portions) to complete the removal of the monomethine dye. The allene perchlorate (38) (3.49 g, 89%) was then washed with ether and dried, giving violet black needles. M.p. 222 - 224 (d) (block preheated to 215°); λ max (acetonitrile) 518 (4.18) 645 (4.60) 705 (4.16) 980 (4.10).

Found C = 64.52 H = 5.70

$C_{22}H_{21}ClN_2O_4$ requires C = 64.00 H = 5.15

CIX$_5$ <u>2,3-Dimethylindolizinium perchlorate with glyoxal in ethanol.</u>

To a boiling solution of 2,3-dimethylindolizinium perchlorate (2.45 g, 0.010 mole) in ethanol (60 mls) wasadded glyoxal (30% $^w/_w$) (3.0 ml ~ 0.0130 mole). The mixture became blue and was heated at the boiling point for 30 seconds by which time the product had precipitated as a mass of black needles. The product was collected and digested twice with hot ethanol (150 ml portions). The <u>allene perchlorate</u> (39) (1.262 g, 61%) was then washed with ether, and dried. A portion recrystallised from acetonitrile as small dark brown needles which slowly decomposed > 225° with melting 228 - 228.5°; λ max. (acetonitrile) 468 (3.90) 612 (4.41) 894 (4.00).

Found C = 63.83 H = 5.31 Cl = 8.47 N = 6.89

$C_{22}H_{21}ClN_2O_4$ requires C = 64.00 H = 5.15 Cl = 8.59 N = 6.79

CIX$_6$ <u>1-Methyl-2-phenylindolizinium perchlorate with glyoxal in ethanol.</u>

Glyoxal (30% $^w/_w$)(1.8 mls ~ 0.0075 mole) was added to a boiling solution of 1-methyl-2-phenylindolizinium perchlorate (1.54 g, 0.005 mole) in ethanol (25 mls). The mixture became a greenish blue, and was heated at the boiling point for 30 seconds. The product which had precipitated as a mass of black needles, was filtered from the cooled solution and digested twice with hot ethanol (150 ml portions). The <u>allene perchlorate</u> (40) (1.004g, 92%) was washed with ether and dried. A portion recrystallised from ethanol as brown black microcrystals which slowly decomposed > 230° ;

λ max. (acetonitrile) = 1070 (sh), 706,647,513, and 242 $m\mu$.

Found C = 69.48 H = 5.56 N = 4.53

$C_{32}H_{25}ClN_2O_4$ requires C = 71.57 H = 4.69 N = 5.22

CIX$_7$ Sodium borohydride reduction of 2,3-dimethyl-1-(2,3-dimethyl-indolizin-1-ylvinylidene) indolizinium perchlorate.

To a suspension of the allene (2.06 g, 0.005 mole) in refluxing ethanol (60 mls) was added portionwise and with stirring, sodium borohydride (0.5 g). Reduction proceeded smoothly to give an orange-yellow solution from which orange-yellow needles deposited. The cooled solution was diluted with water, extracted with ether, and the ether extract was washed several times with water, dried (K_2CO_3), and the solvent was evaporated (apparatus washed with ammonia beforehand) leaving an orange crystalline residue. Recrystallisation from a small volume of acetonitrile gave a mixture of the cis- trans- ethylenes (1.31 g, 83%) as orange needles, m.p. 193 - 210°.

The mixed ethylenes (2.0 g) were taken up in benzene-petrol (1:2) and adsorbed on to a column of alumina (28 x 4.2 cm). Elution was with benzene-petrol (2:1). The eluates were collected in 100 ml fractions, each of which was evaporated to dryness on the water bath at reduced pressure and the resulting residues recrystallised from acetonitrile giving the fractions described below:-

(1) and (2)	40 mgs	Yellow orange needles	m.p. 195 - 197.5° (d)
(3)	89 mgs	" " "	m.p. 206 - 210.5° (d)
(4)	120 mgs	" " "	m.p. 208.5 - 211.5° (d)
(5)	119 mgs	" " "	m.p. 210.5 - 215° (d)
(6) and (7)	147 mgs	" " "	m.p. 208.5 - 215° (d)
(8) and (9)	27 mgs	" " "	m.p. 208.5 - 215° (d)

Fractions (5) to (9) were rechromatographed through a short column with benzene-petrol (2:1). The resulting residue (86 mgs) after evaporation at reduced pressure had m.p. 210.5 - 215.5° (d). A portion of this residue, recrystallised from acetonitrile for analysis, formed yellow-orange needles, m.p. 210.5 - 214° (d); λ max. (acetonitrile) 415 (broad) (4.14) 362 (4.50) 347 (shoulder) (4.27) 300 (point of inflection) (4.10) 255 (4.69) 239 (4.46).

Found C = 83.35 H = 7.42 N = 887

$C_{22}H_{22}N_2$ requires C = 84.04 H = 7.05 N = 8.91

CIX_8 <u>Sodium borohydride reduction of ethanediylidenebis-(1,2-dimethylindolizinium perchlorate).</u>

Sodium borohydride (0.80 g) was added portionwise to a boiling suspension of the diperchlorate (2.567 g, 0.005 mole) in ethanol (120 ml). The reduction proceeded smoothly to give an orange-yellow solution from which orange-yellow flat needles deposited. The cooled solution was diluted with water and extracted with ether. The ether extract was washed several times with water, dried, and the solvent evaporated (apparatus washed with ammonia beforehand). The yield of the crude ethylene was quantitative. The crude material recrystallised from acetonitrile giving a mixture of the _cis-_, _trans-_ ethylenes as orange flat needles (0.985 g, 63%), m.p. 165 - 180° (d).

The product from the reduction of diperchlorate (5.134 g, 0.01 mole) was taken up in benzene-petrol (1:1), adsorbed into a column of alumina (30 x 5.5 cm), and eluted throughout with benzene-petrol. The eluates were collected in (200 ml) fractions each of which was evaporated to dryness on the water bath at reduced pressure and the resulting residue recrystallised from acetonitrile. The following fractions were obtained:

(1) 350 mgs Yellow-orange needles, some crystals appeared deeper orange (similar to those of succeeding fractions) m.p. 179 - 183°.
(2) 700 mgs Thick orange needles m.p. 180 - 183°.
(3) 250 mgs " " " m.p. 180 - 183°.
(4) 110 mgs Thick orange needles m.p. 178.5 - 181.5°.
(5) Contained a minute amount of material and was discarded

A specimen of fraction (2) was recrystallised once from acetonitrile for analysis. λ max (acetonitrile) 410 (4.46), 300 (4.39), 290 (4.39), 245 (4.45), 223 (4.51)

Found C = 83.64 H = 7.02 N = 9.22

$C_{22}H_{22}N_2$ requires C = 84.04 H = 7.05 N = 8.91

CIX_9 <u>Dehydrogenation of 1,1'2,2'-tetramethyl-trans-vinylene-3,3'-di-indolizine with chloranil and perchloric acid.</u>

1,1'2,2'-Tetramethyl-<u>trans</u>-vinylene-3,3'-di-indolizine (0.334 g, 0.001 mole) was added to a boiling solution of chloranil (0.246 g, 0.001 mole) and perchloric acid (0.45 ml, 60%) in acetonitrile (5 mls), and the resulting mixture was refluxed for 2 minutes. On cooling ethanediylidenebis-(1,2-dimethylindolizinium perchlorate) (0.110 g, 21%) crystallised out as dark brown prisms, identical (m.p. and visible spectrum) with the product of condensation of glyoxal with 1,2-dimethylindolizinium perchlorate in acetonitrile.

CIX_{10} <u>Dehydrogenation of 2,2'3,3'-tetramethyl-trans-vinylene-1,1'-di-indolizine with chloranil and perchloric acid.</u>

2,2'3,3'-Tetramethyl-<u>trans</u>-vinylene-1,1'-di-indolizine (0.105 g, 0.00033 mole) was added to a boiling solution of chloranil (0.082 g, 0.00033 mole) and perchloric acid (0.15 ml, 60% ( )) in acetonitrile (3 mls), and the resulting mixture refluxed for 2 minutes. On cooling ethanediylidenebis-(2,3-dimethylindolizinium perchlorate) (0.170 g, 99%) crystallised out as brown prismatic needles, addition of ether to the mother liquors precipitated a second crop of prismatic needles of product, identical (m.p. and visible spectrum) with the product of condensation of glyoxal with 2,3-dimethylindolizinium perchlorate in acetonitrile.

[redacted] [redacted]

Abbreviations Used.

Ann.	Liebig's Annalen der Chemie
Arch. Pharm.	Archiv der Pharmazie
Angew. Chem.	Angewante Chemie
Atti R.A.Lincei	Atti della Reale Accademia dei Lincei
Ber.	Berichte der deutschen Chemischen Gesellschaft (Discontinued with Vol. 77, 1944; continued as Chemische Berichte with Vol. 80, 1947.
Bull. Soc.	Bulletin de la Societe Chimique de France
C.A.	American Chemical Abstracts
Canad. J. Chem.	Canadian Journal of Chemistry
Chem. Ind.	Chemistry and Industry
Chem. Rev.	Chemical Reviews (Published by the American Chemical Society)
Chem. Zentr.	Chemisches Zentralblatt
Compt. rend.	Comptes rendus hebdomadaires des Seances de l'Academie des Sciences
Cotterell	Cotterell, "Strength of Chemical bonds" Butterworths Scientific Publications 1954.
Dewar	Dewar, "The Electronic Theory of Organic Chemistry" 1st Edition, Oxford University Press
Ginsburg	"Non Benzenoid Aromatic Compounds" Edited by David Ginsburg, Interscience Publishers Ltd., 1959.
Helv. Chim Acta	Helvetica Chimica Acta
Izvest Akad Nauk	Izvestiya Akademii Nauk S.S.S.R., Otdelenie Khimicheskikh Nauk Moscow

J.	Journal of the Chemical Society
Jackman	Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry". Pergamon Press
J.A.C.S.	Journal of the American Chemical Society
J.Chem. Phys.	Journal of Chemical Physics
J.Org. Chem.	Journal of Organic Chemistry
J.Pharm.Soc.Jap.	Journal of Pharmaceutical Society of Japan
Nature	Nature
Org. Syn.	Organic Syntheses, Chapman and Hall Ltd.
Pauling	Pauling, "The Nature of the Chemical Bond", Cornell University Press N.Y. 1940
Pitzer	Pitzer, "Quantum Chemistry", Prentice-Hall N.Y., 1953
Phys.Rev	Physics Reviews
Q.Rev.	Quarterly Reviews (Published by the Chemical Society)
Rec.trav.chim.	Recueil des travaux chimique des Pays-Bas
Tetrahedron	Tetrahedron Letters
Trans.Farad.Soc.	Transactions of the Faraday Society
Wheland	Wheland, "Resonance in Organic Chemistry" Wiley N.Y. 1955
Zhur.Obs.Khim.	Zhurnal obshchei Khimii
Z.Physik	Zeitschrift fur Physik
Z.Naturforsch	Zeitschrift fur Naturforschung.

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PLATE I

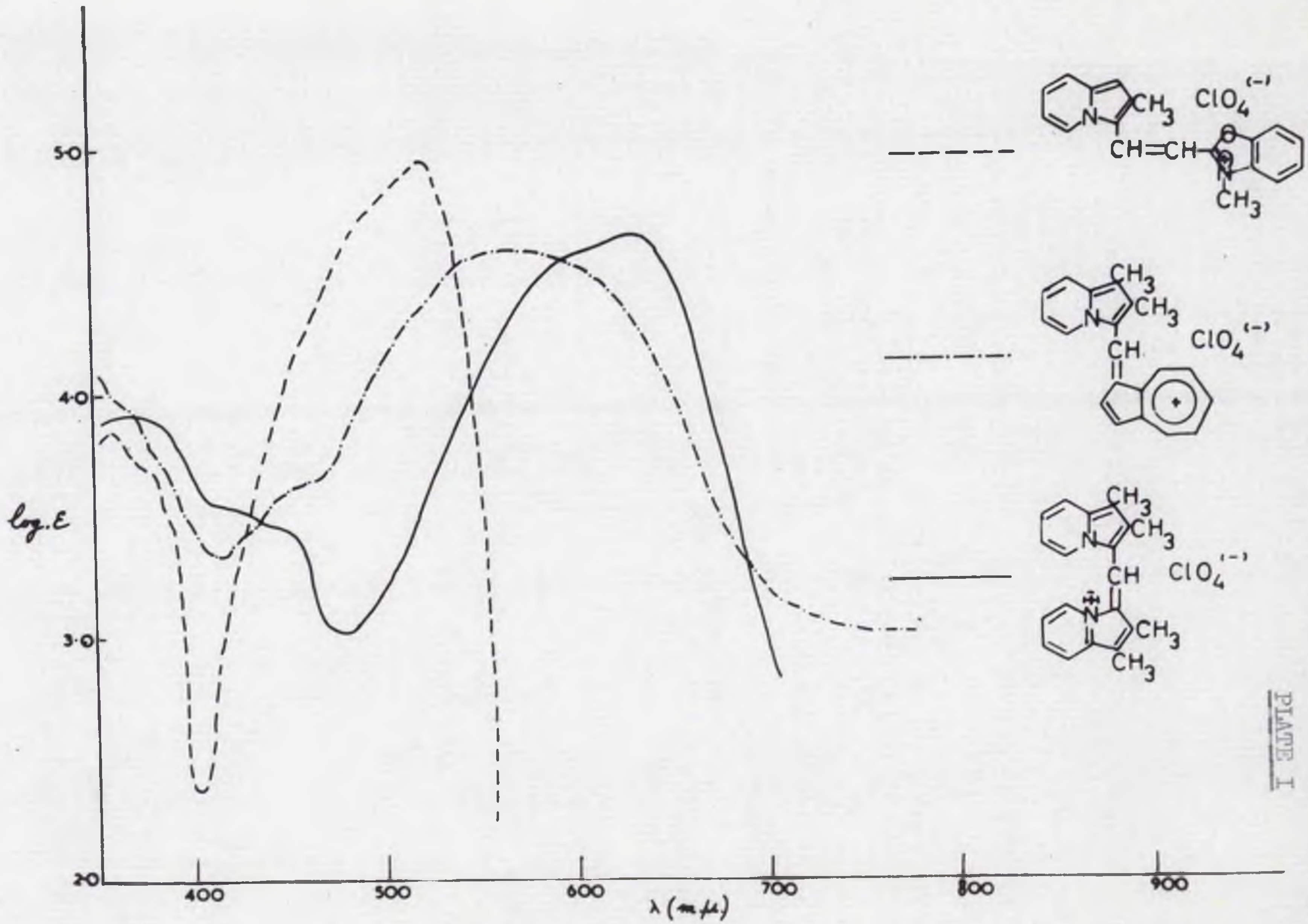

PLATE II

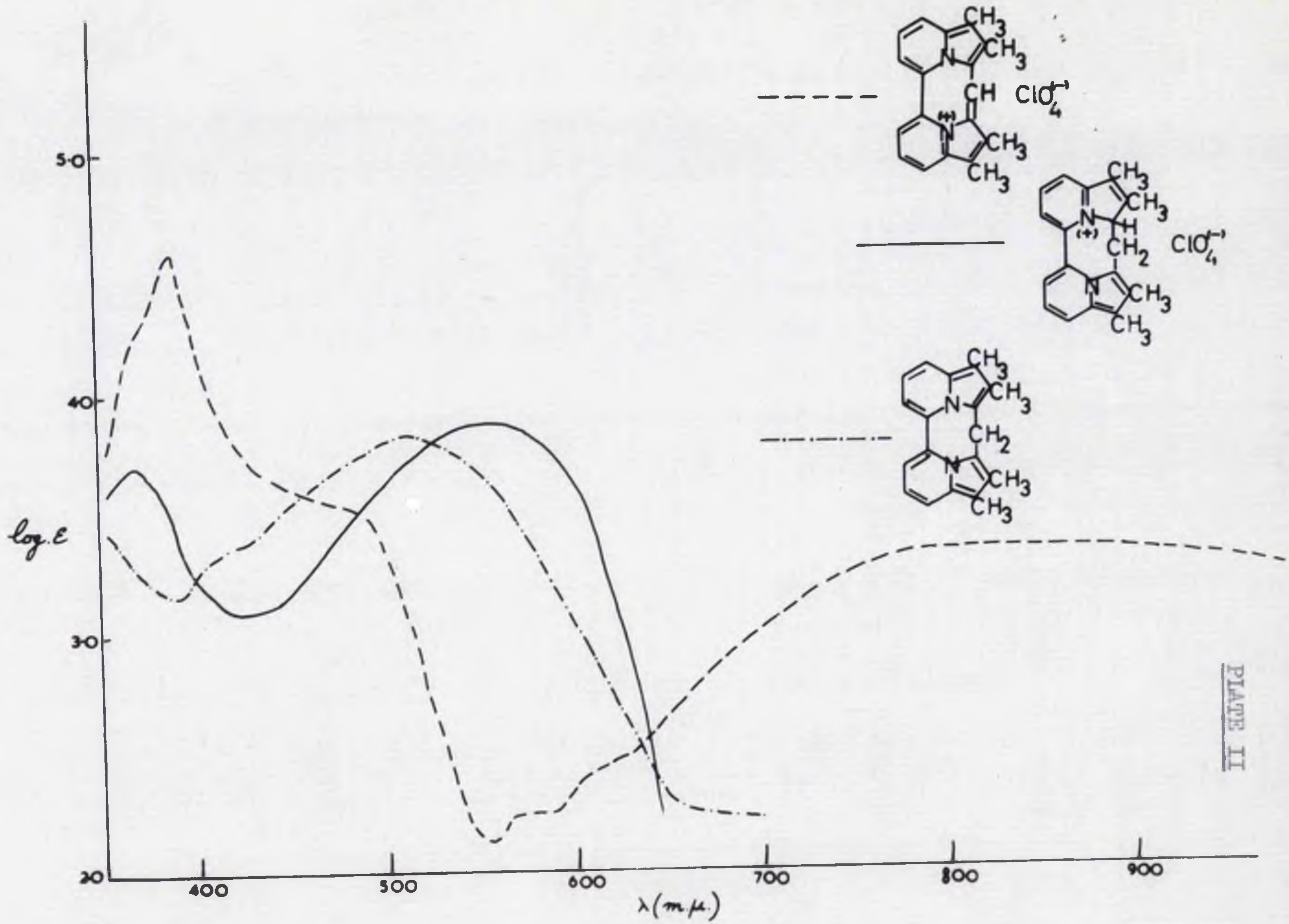

PLATE III